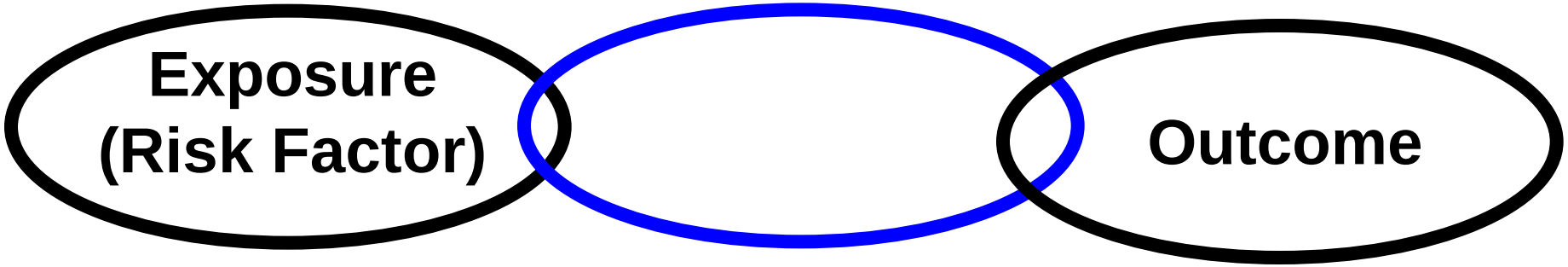
An Overview of Analytic Epidemiology

Association

A link between antecedent factors and some outcome –possibly a causal relationship, but not necessarily.



Exposures
"Risk factors"
Preventive measures
Management strategy
Independent variables

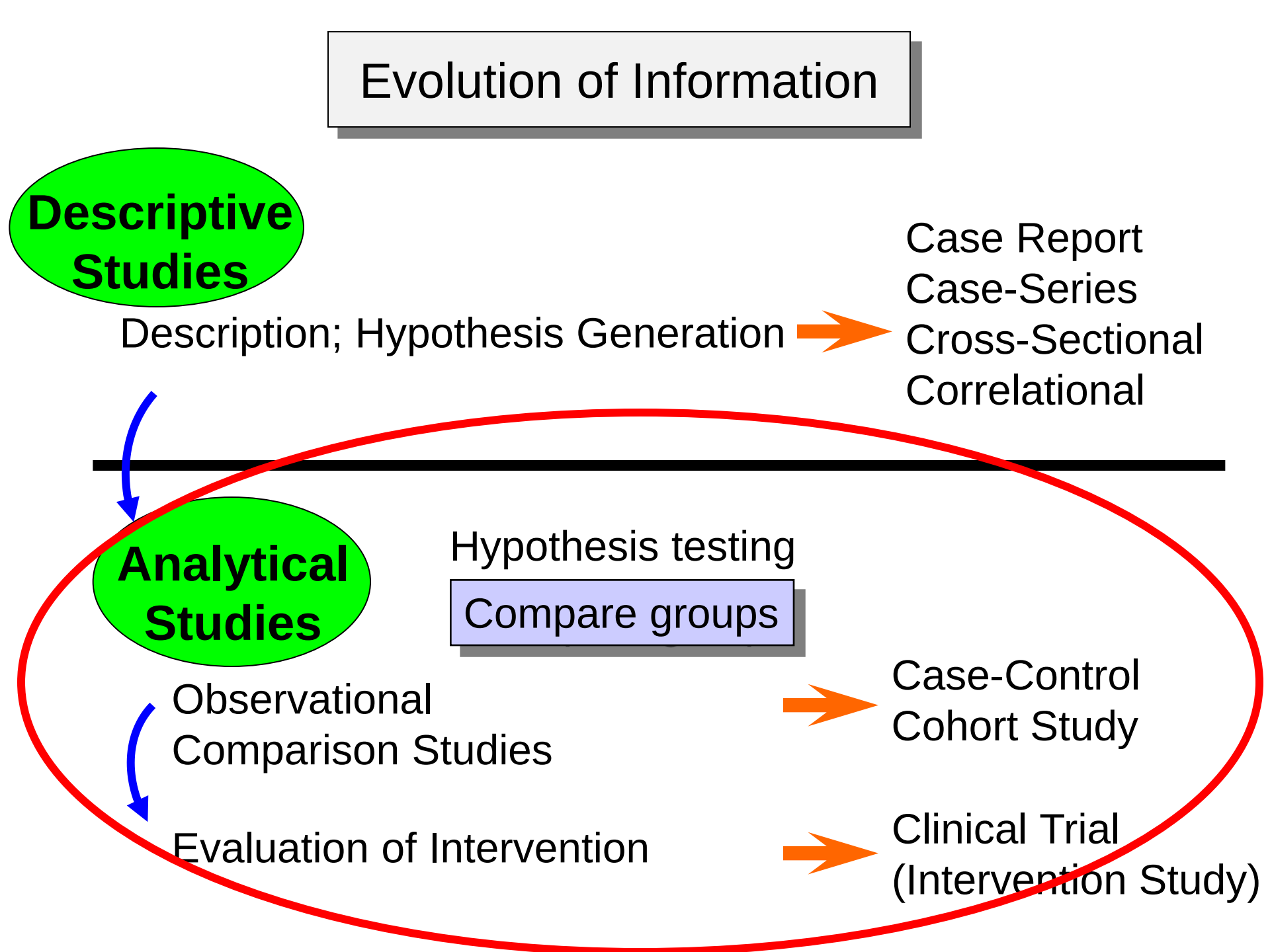
→

Outcomes
Dependent variable
Disease occurrence

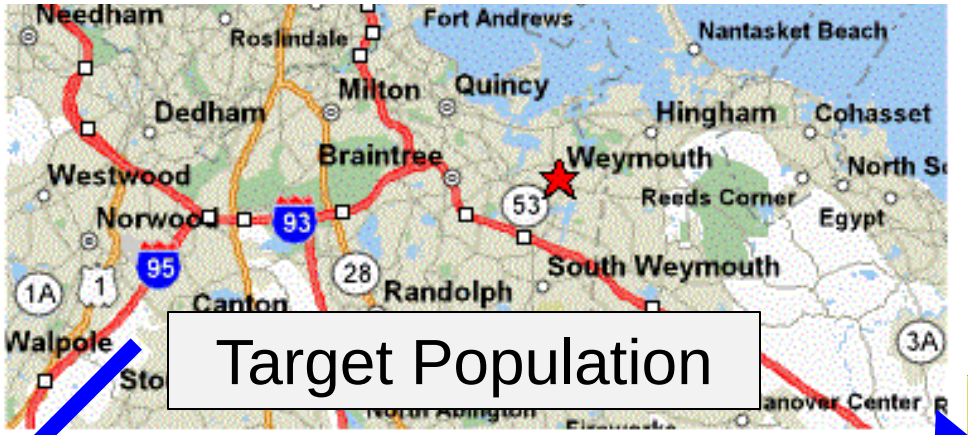
Examples:

Lack of exercise → Heart disease?

Flu Shot → Dystonia Disorder?


Evolution of Information
Descriptive Studies
Description; Hypothesis Generation
Case Report
Case-Series
Cross-Sectional
Correlational
Analytical Studies
Hypothesis testing
Compare groups
Observational
Comparison Studies
Case-Control
Cohort Study
Evaluation of Intervention
Clinical Trial
(Intervention Study)

In analytic studies one enrolls subjects from a population and groups them in some way to make comparisons that test association between risk factors and outcomes.



Sample

Inference

Study Population

Are the results valid?

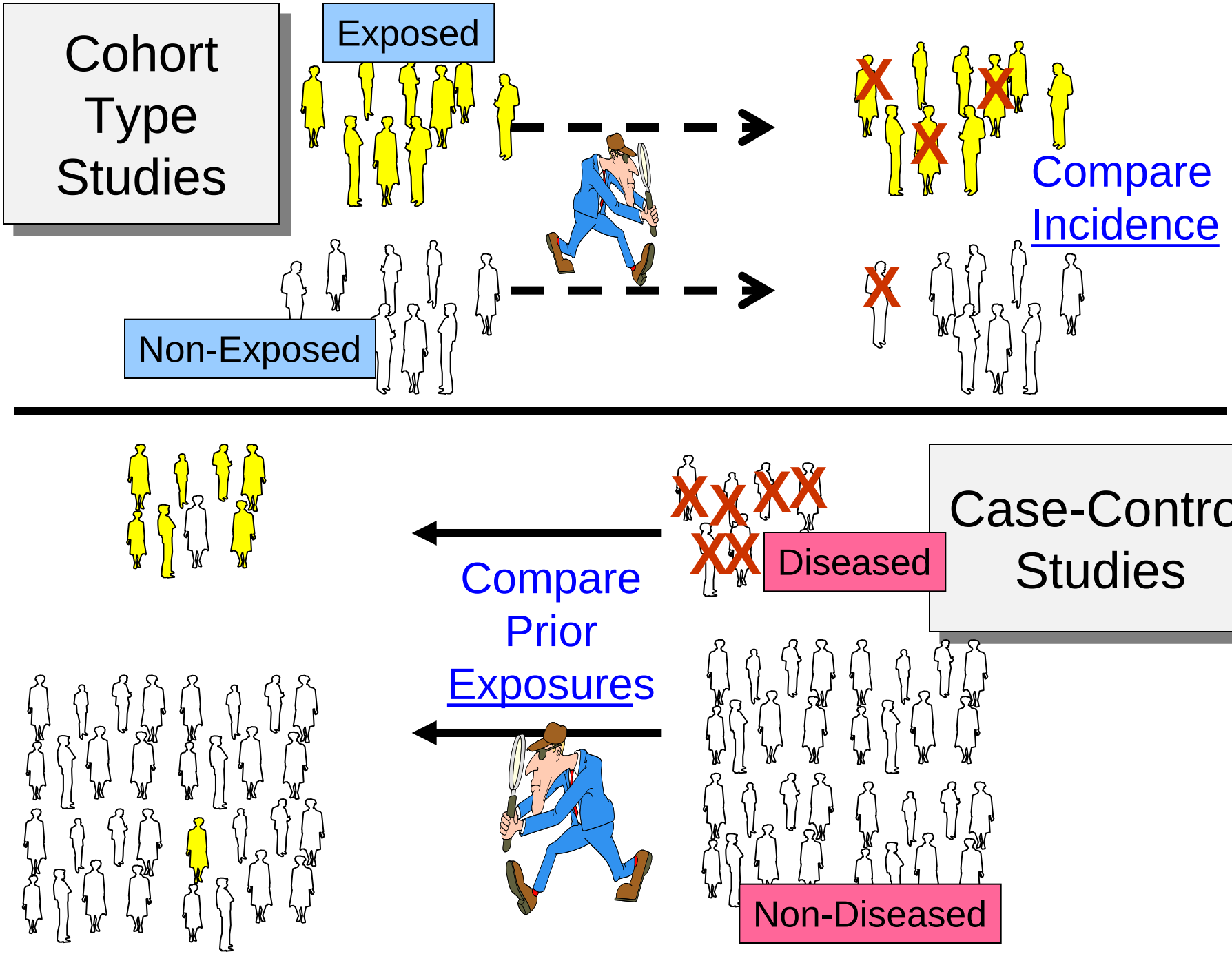
- **Chance**
- **Bias**
- **Confounding**

- **Collect data**
- **Make comparisons**

Is there an association?

Two Basic Strategies for Testing Associations

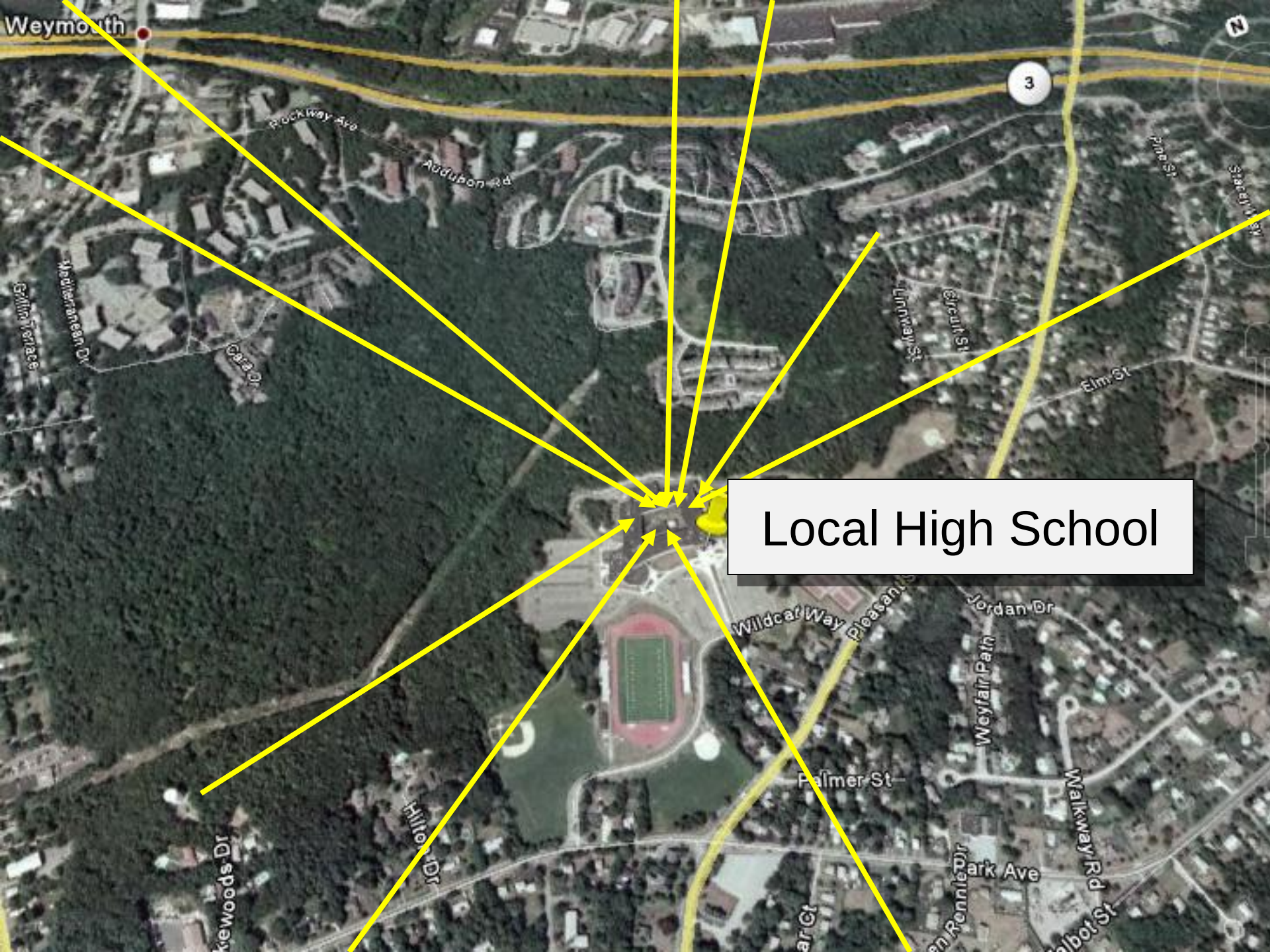
- Cohort type of study
- Case-Control study


Cohort Type Studies
Exposed
Non-Exposed
Compare Incidence
Case-Control Studies
Diseased
Non-Diseased
Compare Prior Exposures

A Salmonella Outbreak

Surveillance system for reportable infectious diseases identifies a case of Salmonella food poisoning.

Subsequent surveillance and active case finding revealed a substantial number of recent cases.


Local High School
Weymouth
Rockway Ave
Audubon Rd
Griffin Terrace
Mediterranean Dr
Gail Dr
Linnway St
Circuit St
Elm St
Pine St
Wildcat Way
Jordan Dr
Wayfair Path
Palmer St
Walkway Rd
Park Ave
Hilton Dr
kewoods Dr

Based on the descriptive epidemiology, it is clear that the parent-teacher luncheon is the source of the outbreak (presumably one of the food dishes).

But which food dish was responsible?

An Intuitive Approach

The attendees of the luncheon constitute a well-defined group (cohort) that is the “source population.” Any of a number of food dishes could have been the “exposure” responsible for causing Salmonella in some members of the cohort.

An intuitive approach would be to ask all attendees in the cohort what they ate (their exposures). Then, for each food dish sort the attendees into those who ate it and those who did not, and then compare the incidence of Salmonellosis (the outcome) in the two exposure groups.

For example:

45 attendees completed the questionnaire which asked whether they had become ill and which dishes they had eaten.

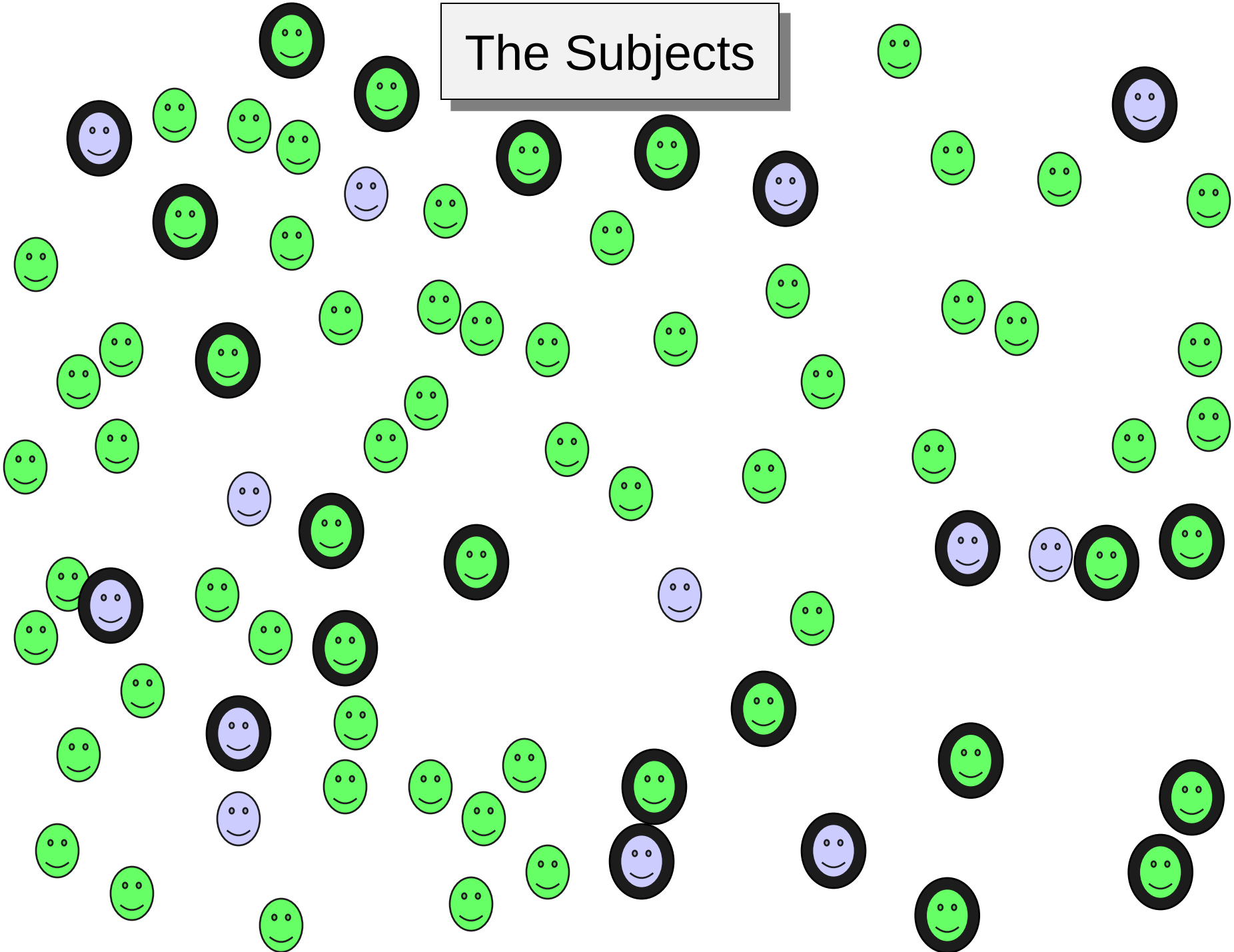
- Among the respondents, 23 reported having eaten a cheese appetizer. 16 of these people became ill.
- 22 denied eating the cheese. 9 of these people became ill?

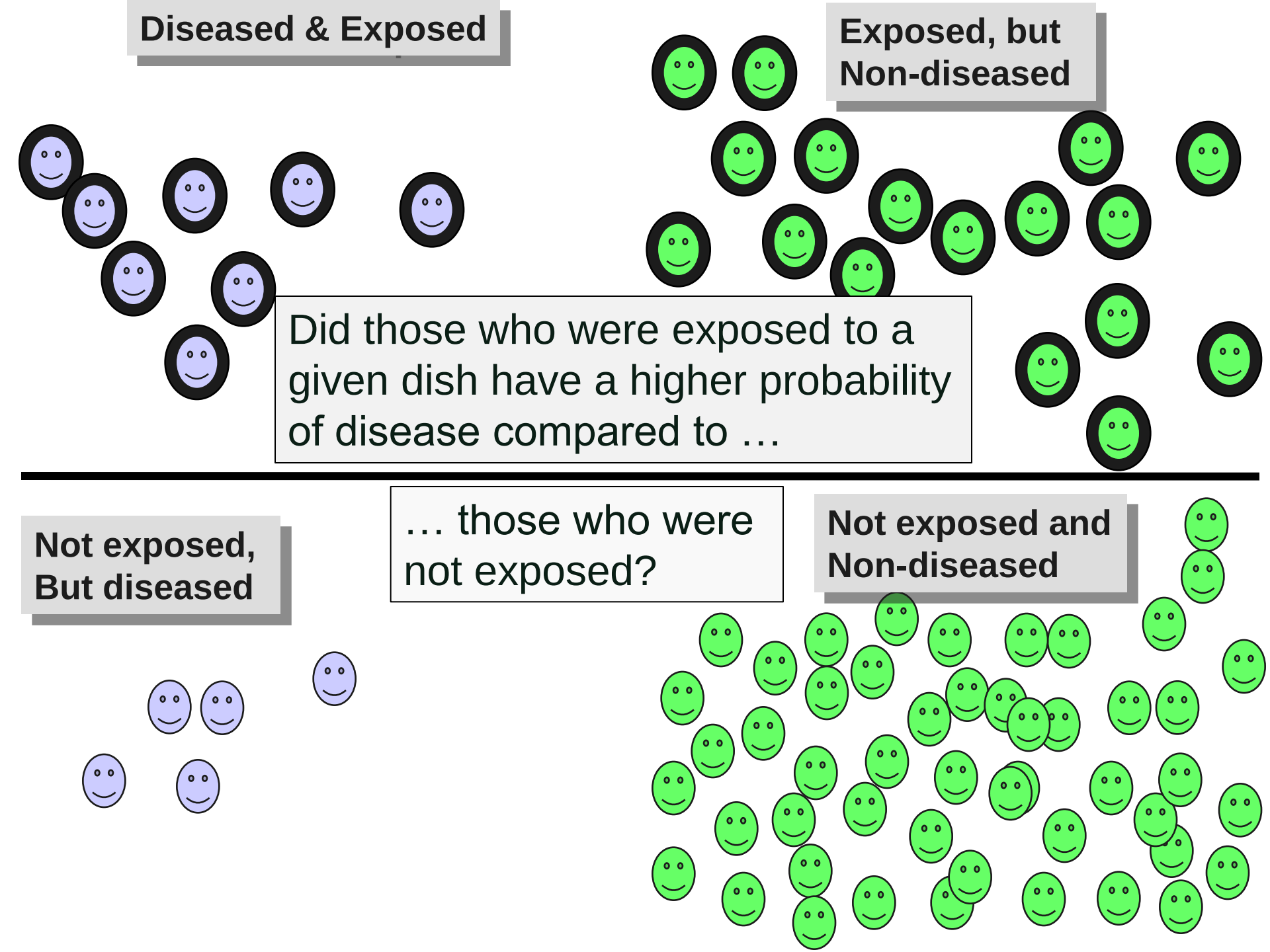
Was the cheese the culprit? Is there evidence of an *association* between eating the cheese appetizer (exposure) and developing Salmonellosis (outcome)?

The Data – A "Line Listing"

ID	gender	Salmonella	Cheese	Mushrooms	Pasta	Pot.Salad	Veg. Lasagna	Chick&Rice	manicotti	Veggies
5	M	No	0	1	1	1	0	1	1	
6	F	Yes	1	1	0	1	0	0	0	
7	F	Yes	1	1	0	0	1	0	1	
8	M	No	0	1	1	1	0	0	0	
9	F	No	0	1	1	1	0	1	0	
10	F	No	1	0	1	0	0	1	0	
11	M	No	1	1	1	0	0	0	0	
12	M	Yes	1	1	1	0	0	0	0	
13	M	No	0	1	0	1	0	1	0	
14	F	Yes	1	0	1	0	0	0	0	
15	M	No	1	1	1	0	0	0	0	
16	M	No	1	0	0	1	0	0	0	
17	F	No	1	0	1	0	0	0	0	
18	M	Yes	1	0	0	0	0	0	1	
19	F	Yes	1	0	1	1	1	0	0	
20	M	No	1	1	1	0	0	1	0	
21	F	No	1	0	1	0	0	1	0	
22	F	Yes	1	1	1	1	0	1	0	
23	F	No	1	1	1	0	1	0	0	
24	F	Yes	0	0	1	1	1	0	0	
25	M	No	0	0	1	1	0	1	1	
26	F	No	1	1	1	0	0	1	1	
27	M	No	0	0	1	1	1	0	0	
28	M	Yes	1	1	1	0	0	0	0	
29	F	Yes	1	1	0	0	0	0	1	
30	F	Yes	1	0	1	0	0	0	0	
31	M	No	1	1	1	0	0	1	1	

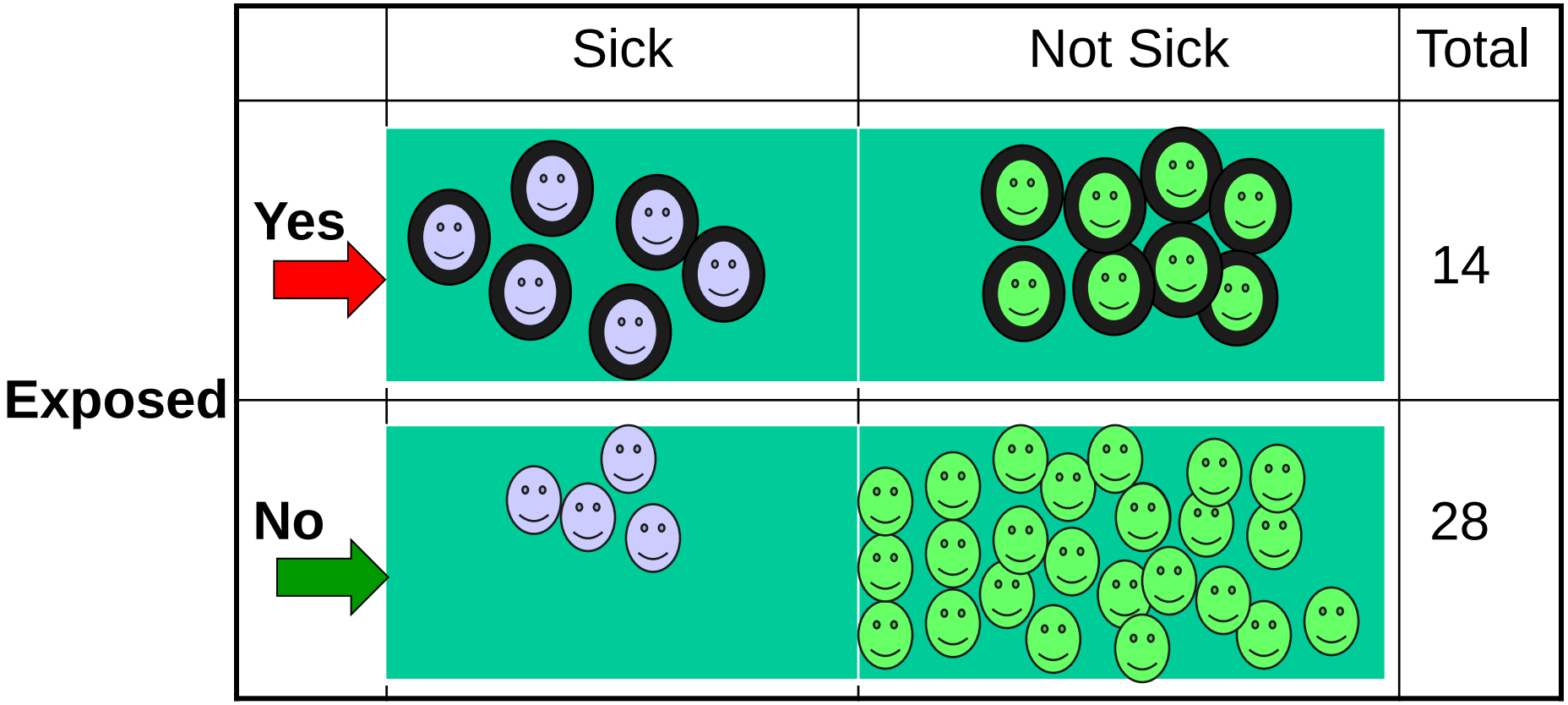
The Subjects




Diseased & Exposed
Exposed, but Non-diseased
Did those who were exposed to a given dish have a higher probability of disease compared to …
Not exposed, But diseased
… those who were not exposed?
Not exposed and Non-diseased

Method #1 for sampling: identify exposed people & non-exposed people and compare their risk of disease.

(Esp. useful for rare ***exposures***, like asbestos.)



Risk in exposed = 6/14 = 43%; risk in unexposed = 4/28 = 14%

Testing the Cheese Appetizer

Salmonellosis

Ate Cheese App.? (Exposed)	Yes	No	
Yes	16	7	23
No	9	13	22

Probability of illness (risk)?

16/23 = 0.70

9/22 = 0.41

How Did the Risks Compare?

Ate Cheese App.? (Exposed)	Salmonellosis: Yes	Salmonellosis: No		Probability of illness (risk)?
Yes	16	7	23	16/23 = 0.70
No	9	13	22	9/22 = 0.41

Risk Ratio = 0.70 / 0.41 = 1.71

Those who ate the chees appetizer had 1.71 times the risk of developing Salmonellosis compared to those who did not eat the cheese appetizer.

The Source?

They looked at each of the "risk factors" (exposures) with a separate 2x2 table. The summary of the results looked like this.

Menu Item	RR
Cheese	1.71
Mushrooms	1.12
Pasta	0.80
Potato Salad	0.54
Veg. Lasagna	0.73
Chicken & Rice	0.66
Manicotti	16.67
Veggies	1.17
Wings	0.74
Caesar Salad	0.26
Kielbasa	1.10
Chick. & Brocc.	1.81
Chicken Parm.	1.17
Calzone	0.81
Eggplant Parm.	0.99
Meatballs	0.74

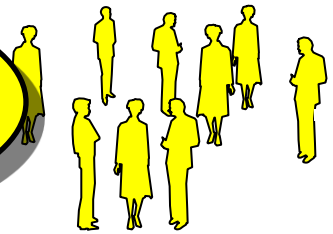
Risk Ratio

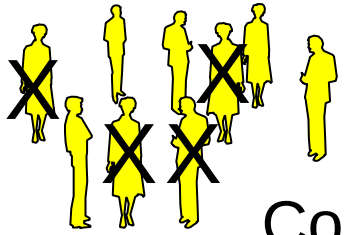
Cohort Study

Key question:

Did people with a particular “exposure” have a greater incidence (risk) of disease?

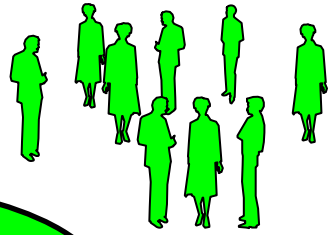
Manicotti

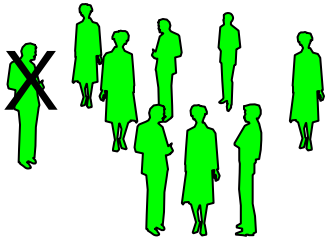




Compare Incidence

Exposure Status

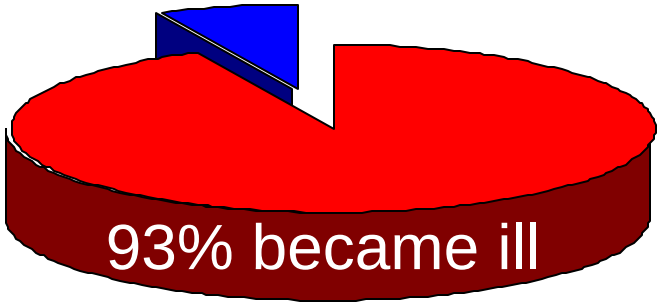


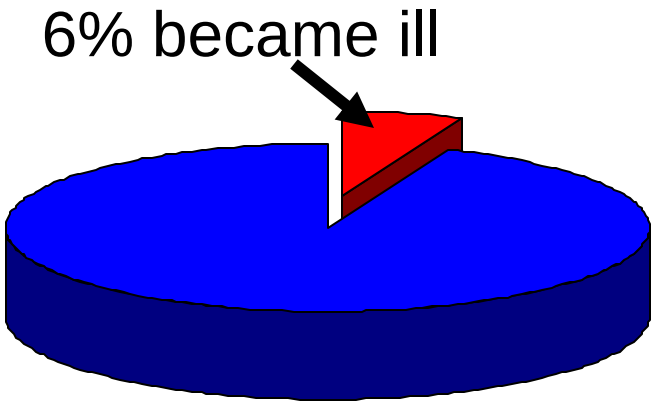


No Manicotti

Did people who ate manicotti have a greater incidence of Salmonella compared to those who did not eat it?

Comparing Incidence - Relative Risk (Risk Ratio)



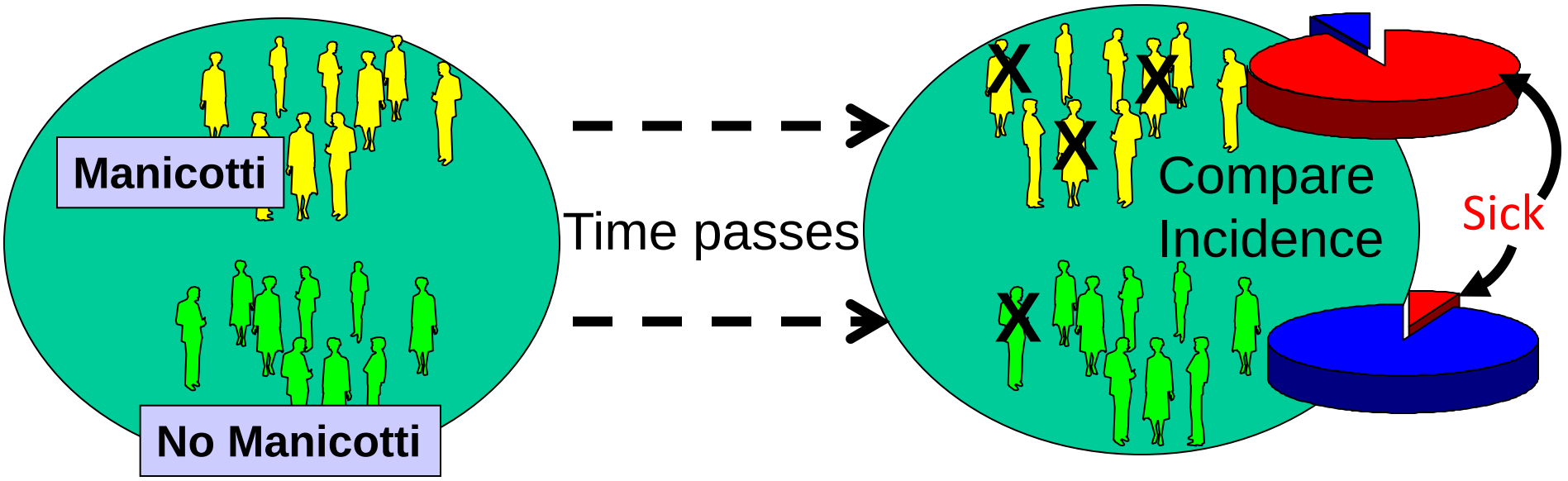


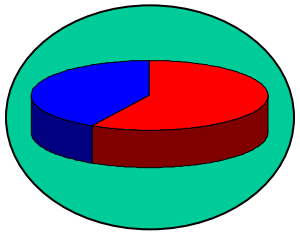
How many times greater was risk in those exposed to manicotti?

$$\text{Risk Ratio} = \frac{93\%}{6\%} = 16.7$$

"The risk of Salmonellosis was 16.7 *times greater* in people who ate manicotti compared to those who didn't."

The Cohort:
People Attending the Luncheon





A small, well-defined cohort.

- The ***source population was small and discrete*** (attendees of appreciation luncheon) & there was the ability to contact all members of the cohort or a substantial proportion of them.
- They could list all foods served at the luncheon & ask each respondent which foods they ate & whether they got sick.
- They could, therefore, determine the exposure status & outcome status for the majority of the cohort. So, they could calculate incidence and RR for each food item.
- The disease was ***common***; 58% of the cohort got it.

Hepatitis Outbreak in Marshfield, MA

- "Between February 25 and 27, 2004 six cases of HAV infection in Marshfield residents were reported to …MDPH. In addition, a case of hepatitis A in a Plymouth resident, employed in Marshfield, was reported." (eventually there were 20 cases).

- Marshfield had 1 case in 2002 and 0 cases in 2003

- "The increase in the number of reported cases … during February in a confined geographic area was an indication of a possible outbreak of hepatitis A infection."

Hepatitis A Facts

Abrupt onset: fever, malaise, anorexia, nausea, and abdominal discomfort; sometimes diarrhea. Jaundice may follow. May be asymptomatic. Infected humans (symptomatic or not) shed the virus into stools.

Transmission: fecal-oral route (ingesting the virus)

- food contaminated by an infected food worker
- produce irrigated/processed with contaminated water
- shellfish from contaminated water
- drinking feces-contaminated water
- sexual: (e.g., oral-anal contact).

Incubation period: 15–50 days (avg.= 28–30).

Most infectious from 1–2 weeks before symptoms until 1 week after.

Descriptive Phase

(generate hypotheses about the source)

Their Suspects (Hypotheses)

Based on these clues:

- Knowledge of biology of hepatitis A (transmission, incubation)
- Time course: epidemic curve of “point source”
- Diverse age, occupation, location
- Interview with a series of cases & similarities in restaurant use

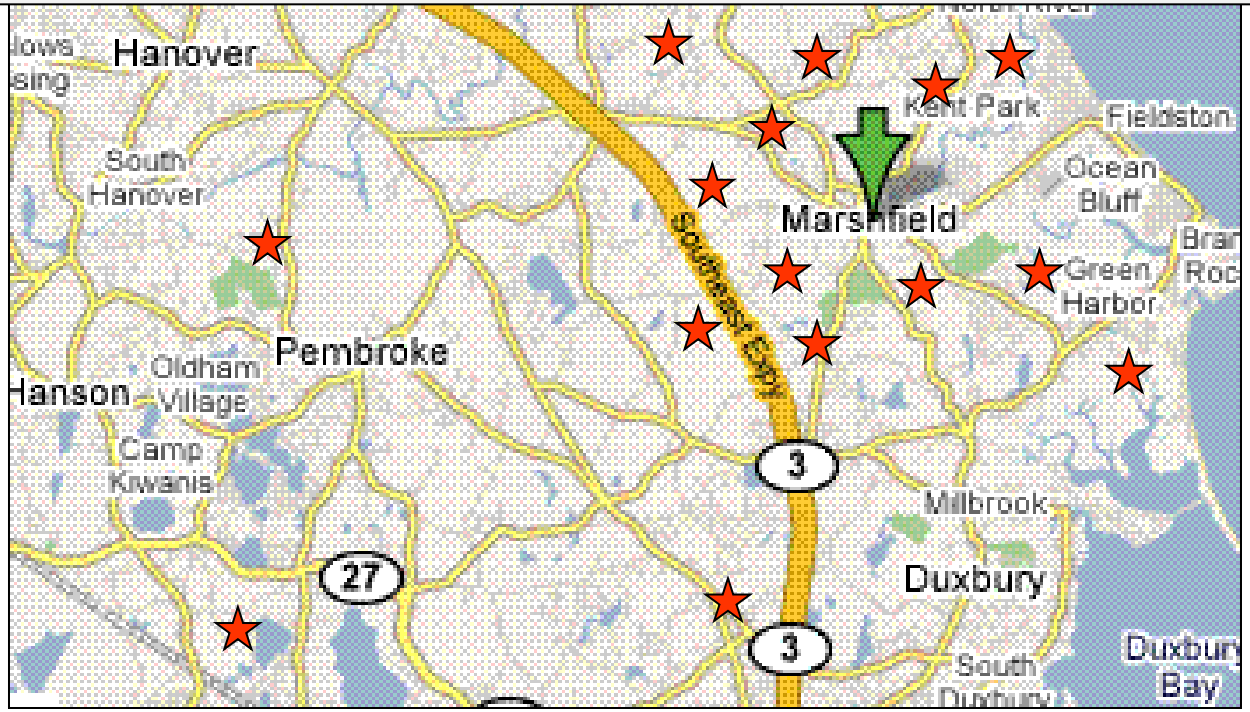
They hypothesized that the source was probably an infected food handler at:

- Rick’s Deli
- McDonald’s
- Jaime’s Pub
- Papa Gino’s
- Friendly’s

Was it feasible to test these hypotheses with a cohort study?

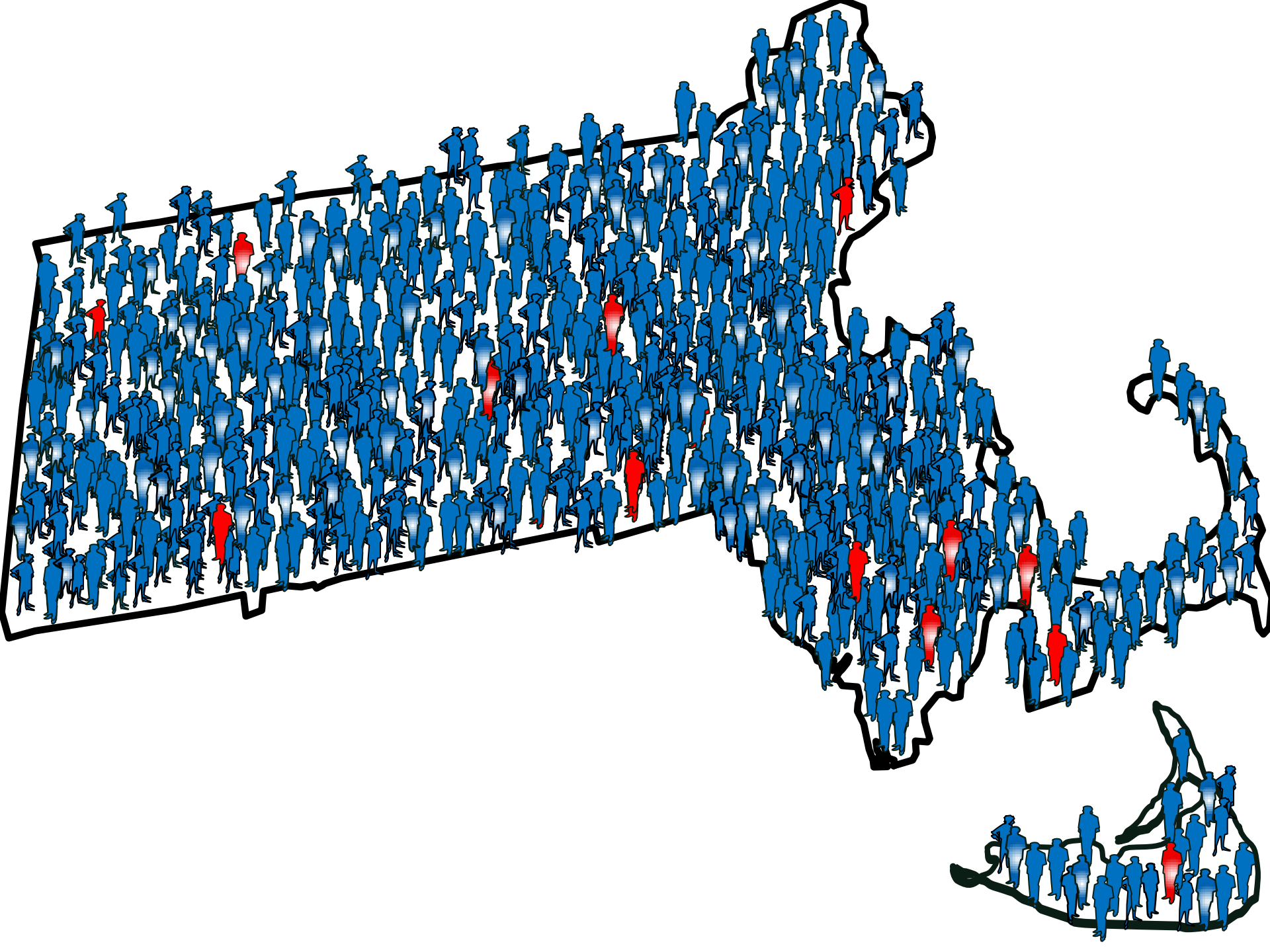
Hepatitis Outbreak – Problems

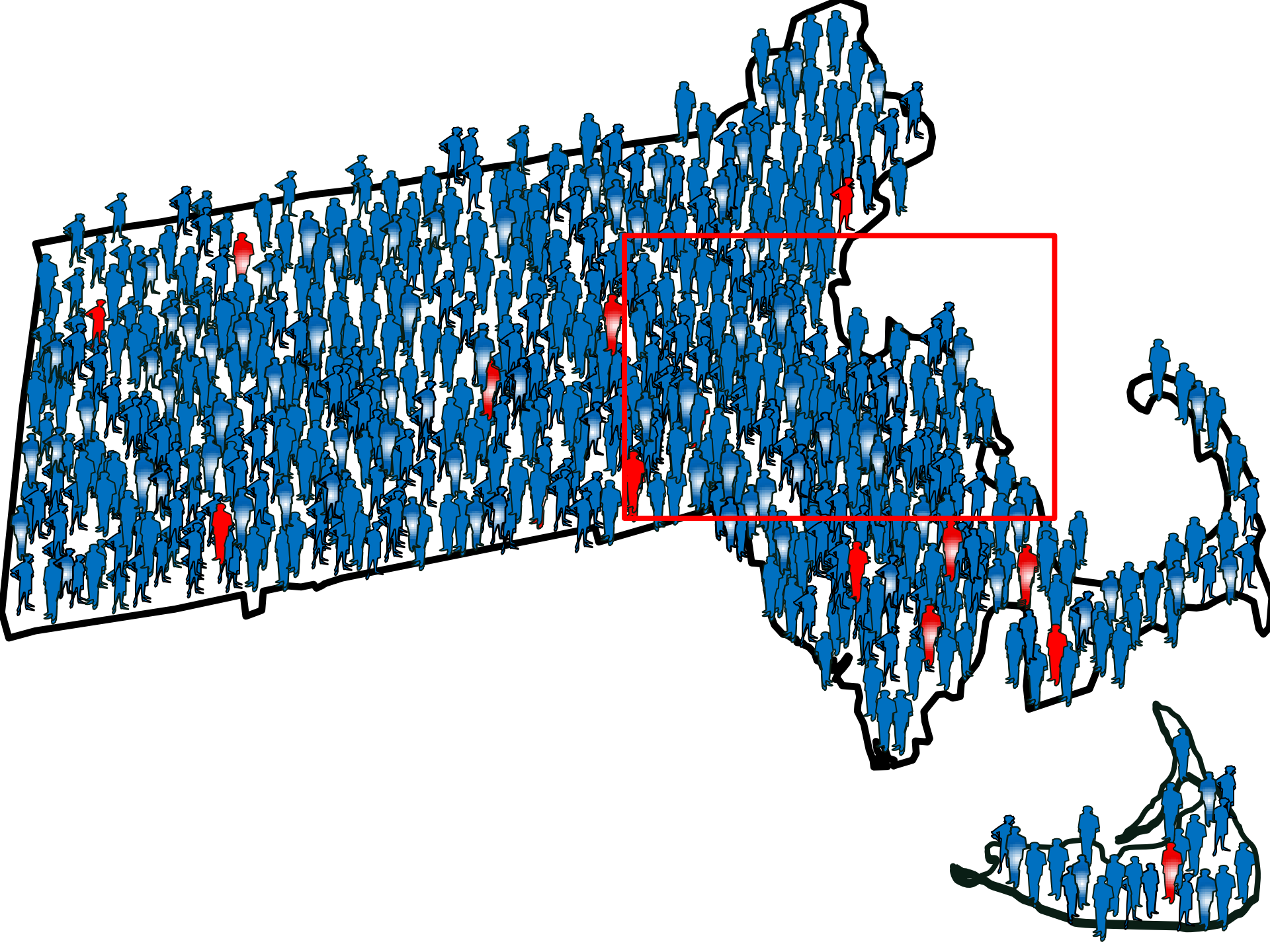
- No clear cohort and only a small # of cases scattered across South Shore. (*rare outcome*)
- No obvious event/place that tied them all together. The source population was large & diffuse with unknown borders, and ***only 20 cases*** had been identified.
- They couldn't interview all residents of MA South Shore.



The Disease Was Uncommon

Of the thousands of people exposed at the responsible restaurant, only a small % became ill. So if we took a random sample of people who ate at each restaurant, the incidence might be 0 even in the offending restaurant.





The Situation

1. The disease is rare.
2. There are many exposed individuals, but most of these are not diseased.
3. Yet, the proportion of exposed individuals among the disease cases may be higher than the proportion of exposure among the controls. (There may be an association.)

Analysis of a Rare Disease

If I somehow had exposure and outcome information on all of the subjects in the source population and looked at the association using a cohort design, it might look like this:

	Diseased	Non-diseased	Total
Exposed	7	1,000	1,007
Non-exposed	6	5,634	5,640

If we are calculating the risk ratio, the key information is the exposure distribution in the disease cases relative to the exposure distribution in the total population.

If we are calculating the risk ratio, the key information is the exposure distribution in the cases relative to the exposure distribution in the total population. And the exposure distribution in non-diseased people is similar to that in the total population.

	Diseased	Non-diseased	Total
Exposed	7	1,000	1,007
Non-exposed	6	5,634	5,640

$$\frac{(7/1007)}{(6/5640)} = 6.53$$

$$\frac{(7/6)}{(1007/5640)} = 6.53 \rightarrow \frac{1.16667}{0.1785} = 6.53$$

If the key information is the exposure distribution in the cases relative to the exposure distribution in the total population, then we could just take a sample of the non-diseased people in order to estimate the exposure distribution in the total population.

	Diseased	Non-diseased	Total
Exposed	7	10	?
Non-exposed	6	56	?

$$\frac{(7/1007)}{(6/5640)} = 6.53$$

$$\frac{(7/6)}{(10/56)} = 6.53 \rightarrow \frac{1.16667}{0.1785} = 6.53$$

In other words, if I want to estimate a risk ratio for a rare disease, it is more efficient to find cases, but then just take a sample of non-diseased "controls" in order to estimate the exposure distribution in the entire population.

	Diseased	Non-diseased	Tot.
Exposed	7	1000	1007
Non-exposed	6	5634	5640

	Diseased	Non-diseased	Tot.
Exposed	7	10	?
Non-exposed	6	56	?

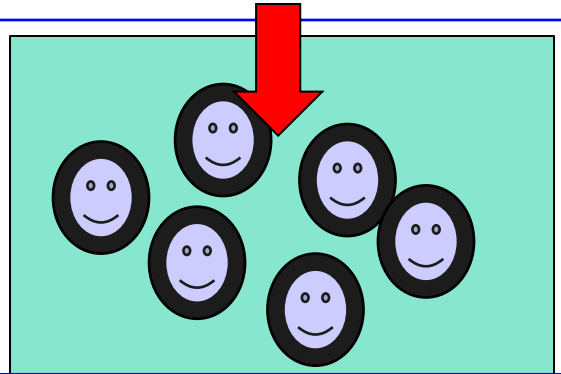
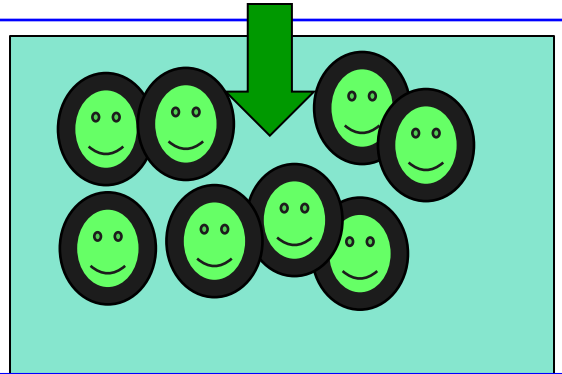
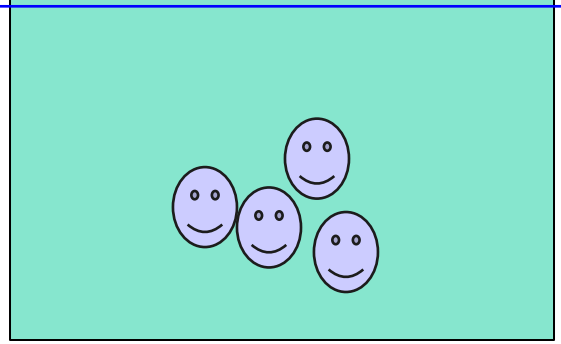
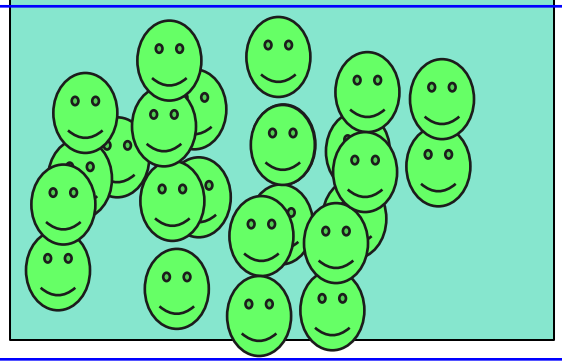
$$\frac{(7/1007)}{(6/5640)} = 6.53 = \text{Risk Ratio} \qquad \frac{(7/6)}{(10/56)} = 6.53 = \text{Odds Ratio}$$

Method #2 for Sampling

Enroll diseased people & non-diseased people and compare their odds of having been exposed.

(Esp. useful for rare ***outcomes***, e.g., birth defects.)

Outcome

Exposure Status	Sick	Not Sick
Yes		
No		

Odds of exposure = 6/4; odds of exposure =8/24

With no defined cohort and a rare outcome, the case-control strategy is much more efficient:

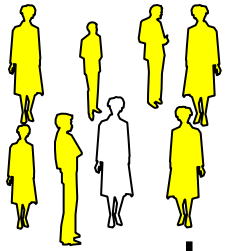
Find as many *sick people (cases)* as you can and ask them about all their exposures (where they ate). Then find *non-affected people* (controls) and ask them about the same exposures.

You can't measure incidence, but you can measure the odds of exposure to each restaurant in the cases (sick people) and compare to the odds of exposure in well people (controls).

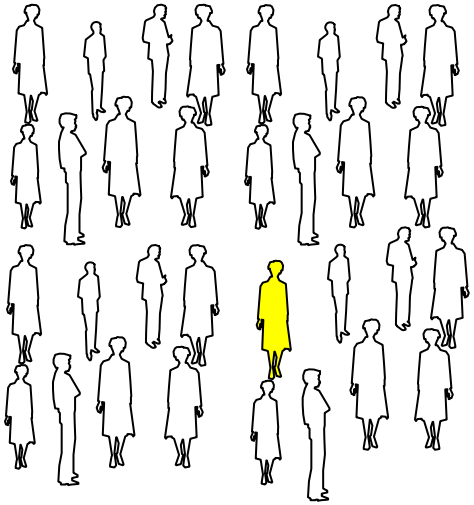
Case-Control Study

Design:

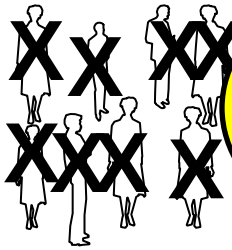
- **Find cases with disease; find non-disease ‘controls’.**
- **Compare the groups with respect to <u>past exposures</u>.**



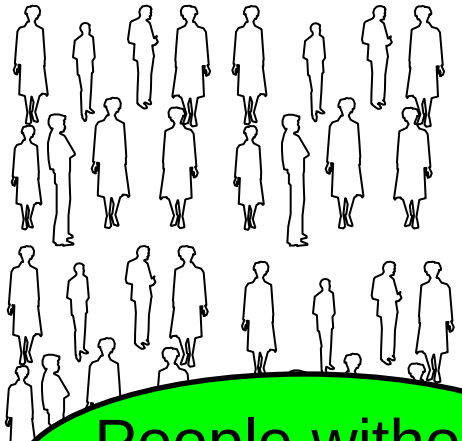
Compare odds of eating at ….



Assess Prior Exposures

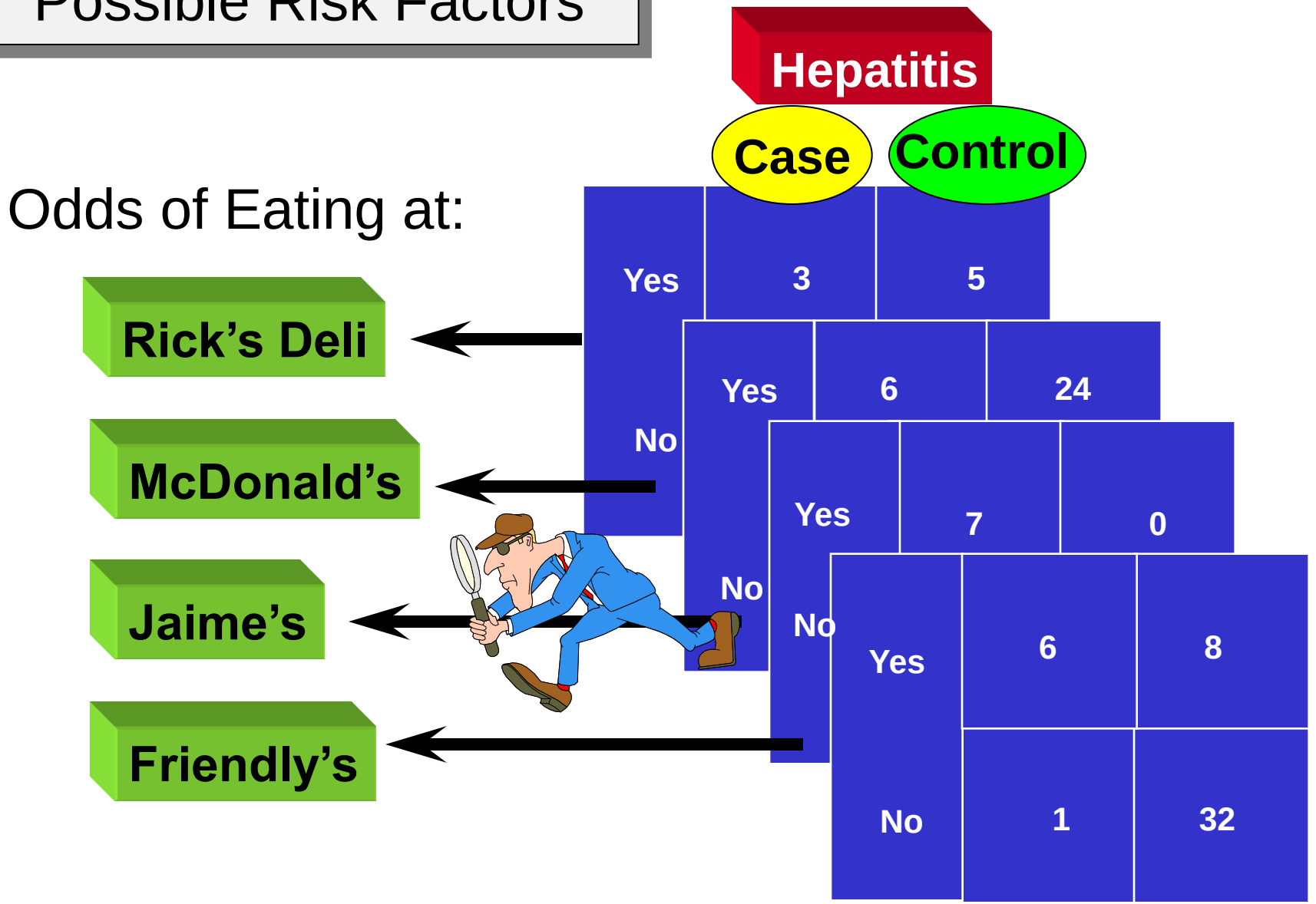


People with Hepatitis A (cases)

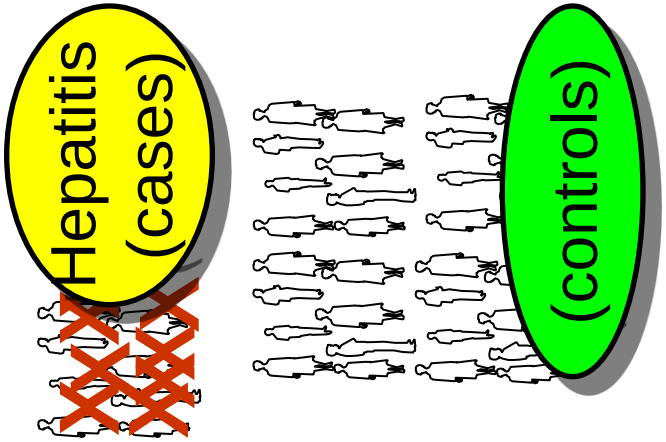


People without it (controls)

Evaluating Multiple Possible Risk Factors



Marshfield Hepatitis Outbreak



Hepatitis

Ate at Rick's Deli	**Cases**	**Controls**
Yes	**18**	**7**
No	**1**	**29**

18 ate at Rick's **1 didn't** **Odds = 18/1**	**7 ate at Rick's** **29 didn't** **Odds = 7/29**

The Odds Ratio

Hepatitis

Ate at Rick's Deli?	Cases	Controls
Yes	**18**	**7**
No	**1**	**29**
	19	**36**

Those who ate at Rick's Deli had 75 times the risk of getting hepatitis A compared to those who did not eat there.

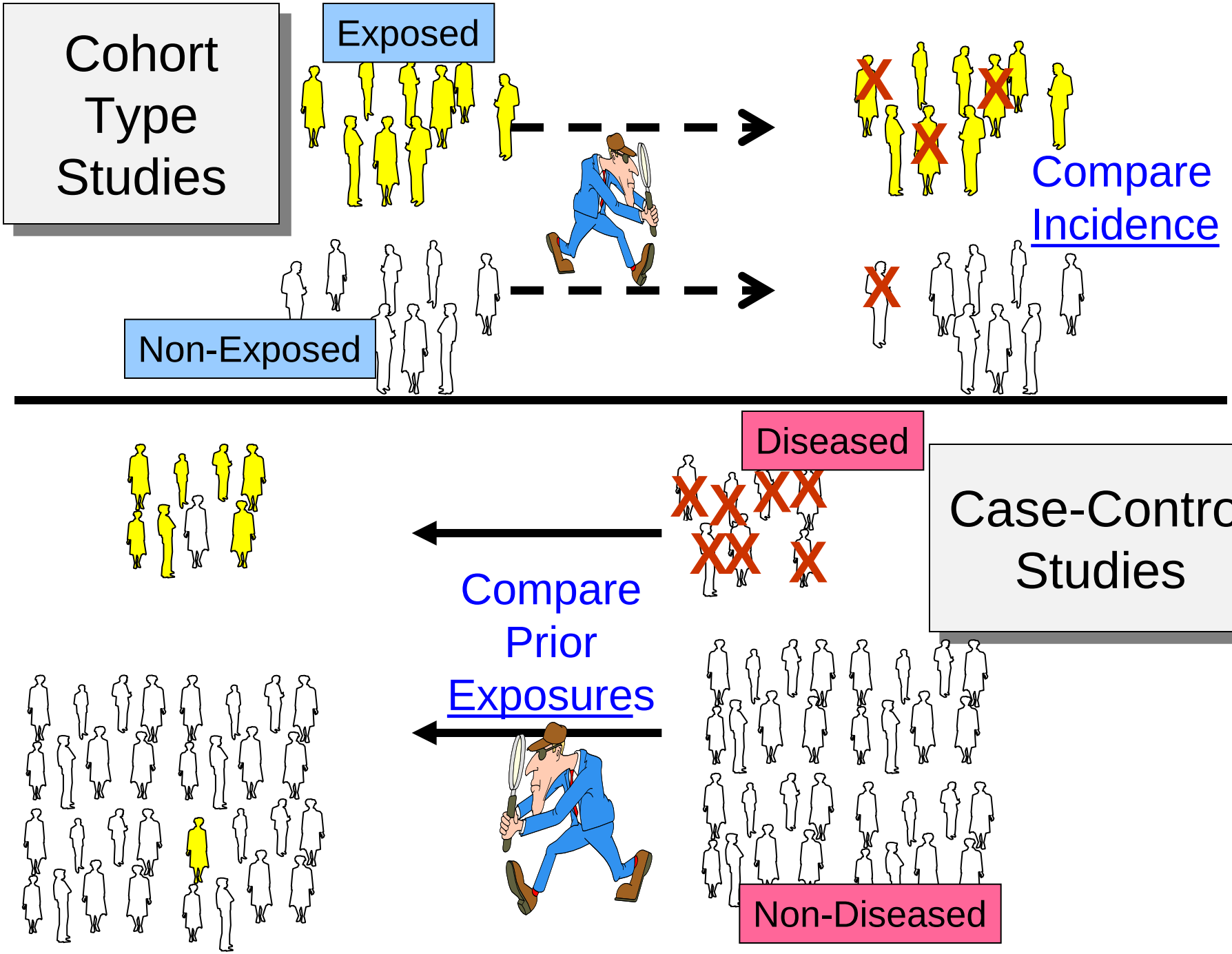
Odds of exposure: → 18/1 7/29

$$\text{Odds Ratio} = \frac{18/1}{7/29} = 75$$

Results in Marshfield

Results:

Rick's Deli	***Odds Ratio = 74.6***
McDonald's	***Odds Ratio = 3.5***
Jaime's Pub	***Odds Ratio = 2.4***
Papa Gino's	***Odds Ratio = 1.1***
Friendly's	***Odds Ratio = 0.8***

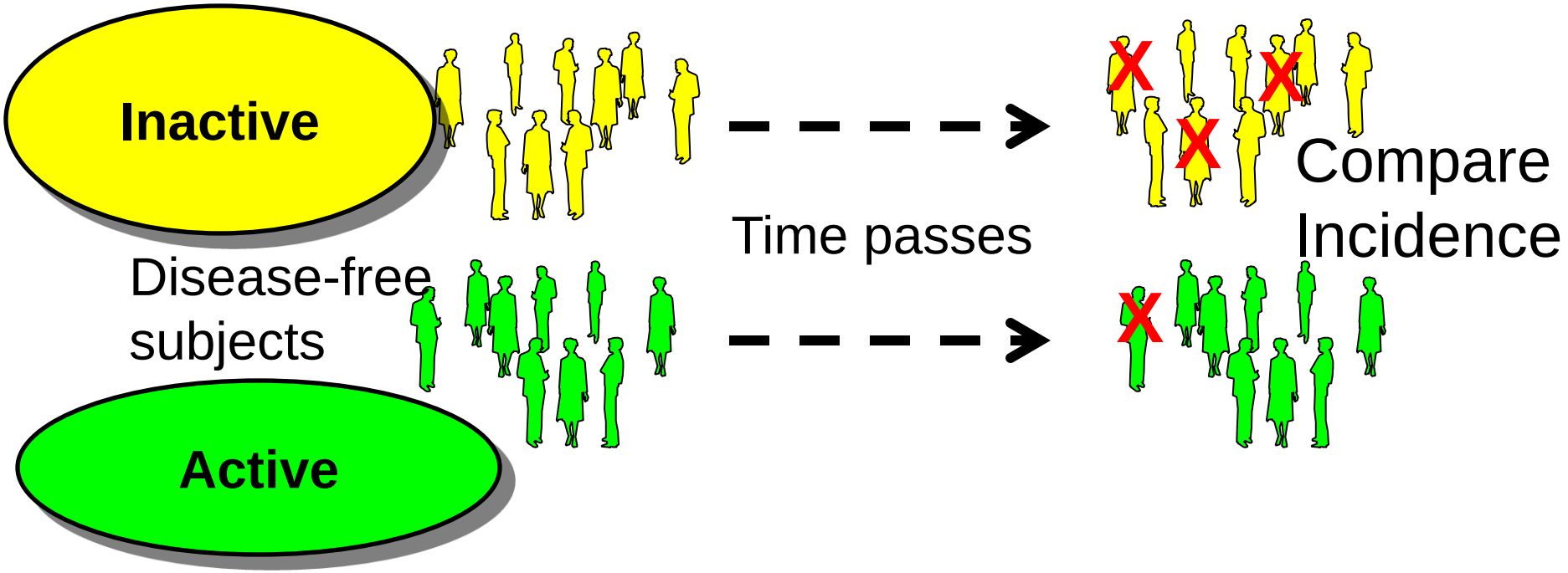

Cohort Type Studies
Exposed
Non-Exposed
Compare Incidence
Diseased
Case-Control Studies
Compare Prior Exposures
Non-Diseased

Is There an Association Between Physical Inactivity and Heart Disease?

Heart disease is a chronic disease.

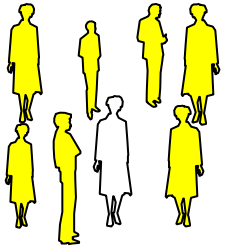
Which study design should we use?

We could use a cohort type of design.



A difference in incidence suggests that the exposure is associated with the disease.

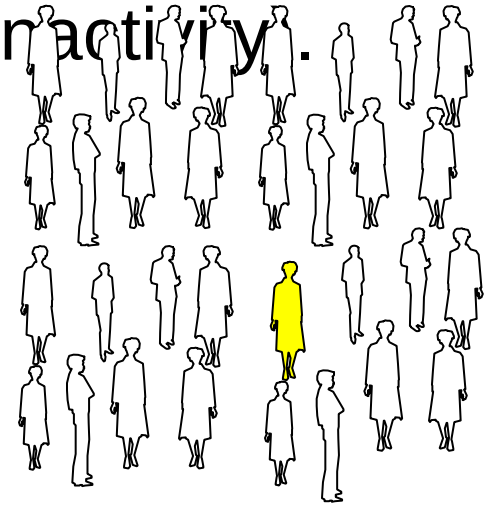
Or we could use a case-control design.

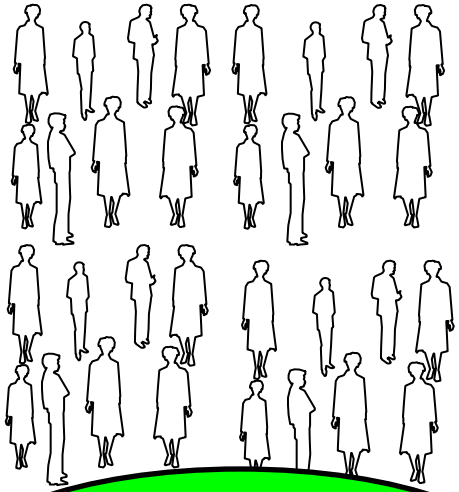


People with CAD (cases)

Compare odds of exposure (inactivity).

“Were you inactive?”





People without CAD (controls)

Choice of study design will depend on:

- degree of existing knowledge,
- whether the outcome is rare,
- whether the exposure is unusual,
- resources, time, money.

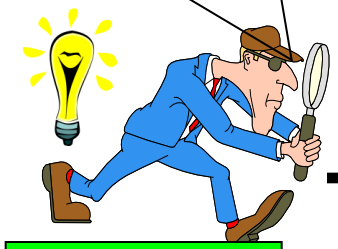
A Prospective Cohort Study

The Cohort

117,000 Nurses *without* cancer or CVD

After time has elapsed investigators use the prospectively collected data to answer many questions.

We need to understand determinants of heart disease in women.



Start of Study

Enroll & assess exposures at the beginning.

Obese

Lean

Compare incidence of heart attack

Follow-up

The study is *planned & designed to answer questions* in a specific area. Non-diseased subjects meeting eligibility criteria are enrolled. Detailed baseline information on lifestyle & exposures is collected from each & they are followed over time.

A Retrospective Cohort Study

The Cohort

Employees of a tire manufacturing company.

Do chemicals used in tire manufacturing increase risk of death?

Get employee health records.

Exposed → ✝✝✝✝✝

Not exposed → ✝ ✝ ✝

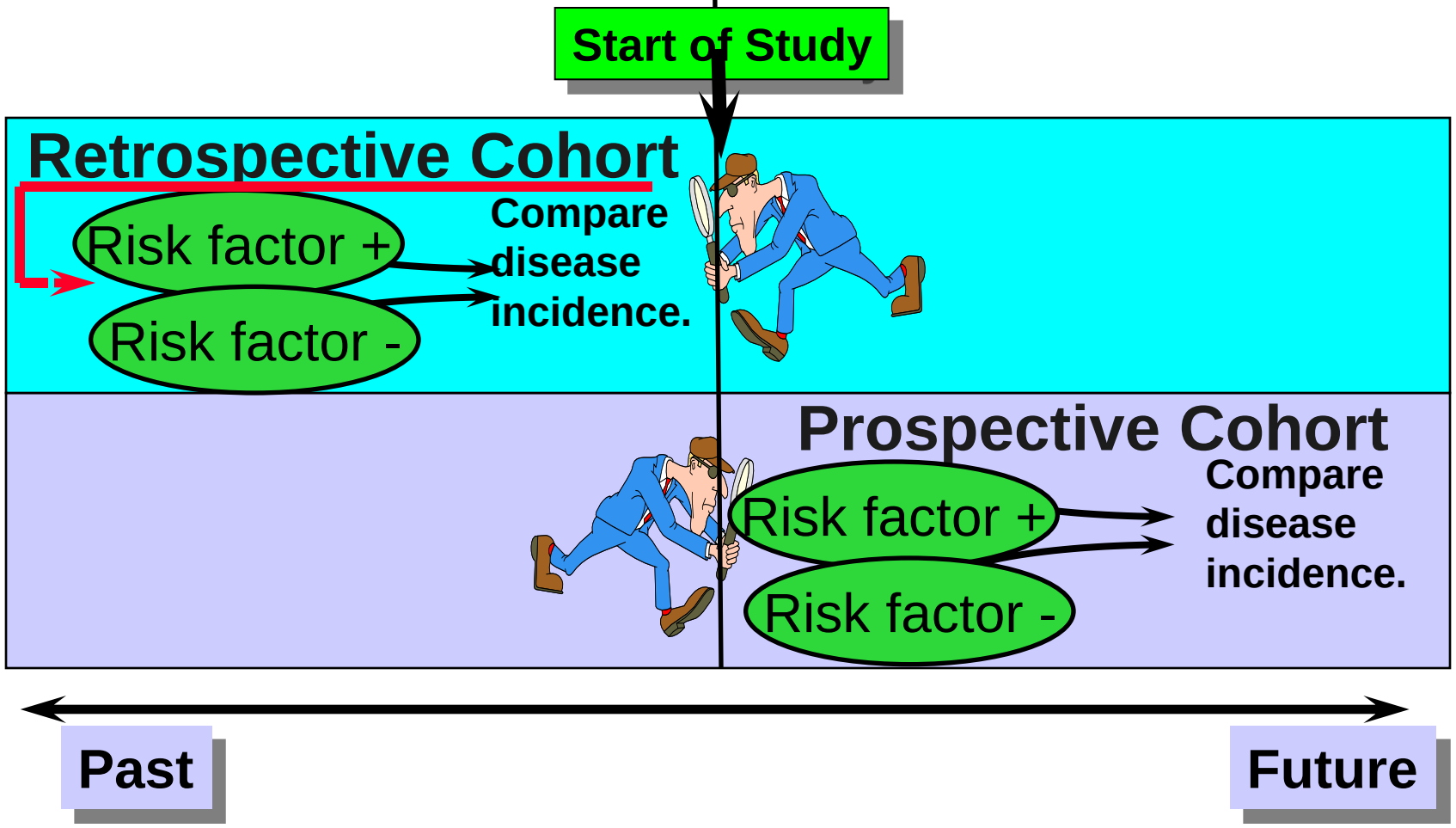
Compare incidence of death

This study was not preplanned. The investigator has to go back to pre-existing data that was not necessarily acquired in a precise, predetermined way. Follow up may have been incomplete.

Past

Start of Study

Retrospective vs. Prospective Cohort Studies



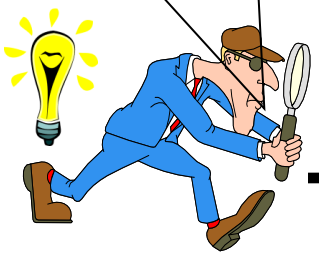
A Prospective Cohort Study

The Cohort

117,000 Nurses *without* cancer or CVD

After time has elapsed investigators use the prospectively collected data to answer many questions.

We need to understand determinants of cancer and CHD in women.



Enroll & assess exposures at the beginning.

obese

lean

Compare incidence of heart attack

Follow-up

Start of Study

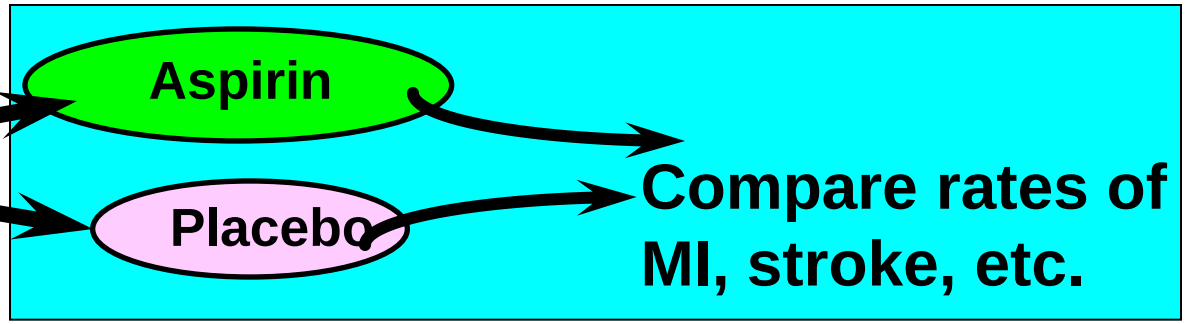
Future

A Randomized Clinical Trial (Intervention Study)

Similar to a prospective cohort study, but the investigator *assigns* exposure (treatment).

Example: Does low-dose aspirin reduce risk of myocardial infarction (heart attack)?

Randomly assign subjects to a treatment or "risk" group

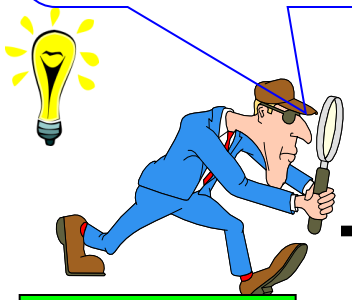


A Clinical Trial

22,000 male MDs without CVD

After time has elapsed investigators use the prospectively collected data to answer many questions.

Does low-dose aspirin prevent heart attacks?



Enroll & *assign exposure* (treatment) at the beginning.

Aspirin

Placebo

Compare incidence of heart attack

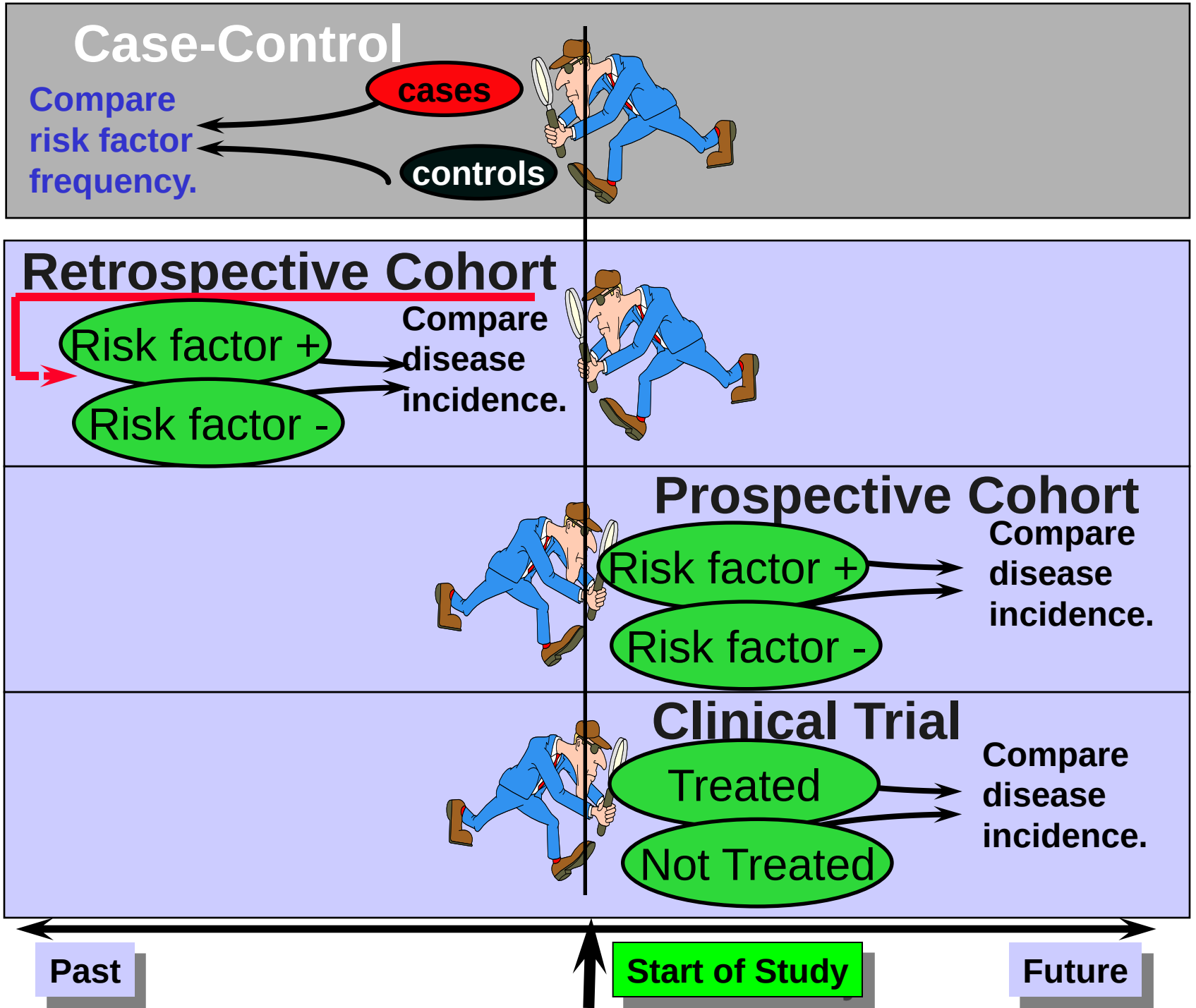
Follow-up

Start of Study

Fatal Myocardial Infarction

	Yes	No		Incidence
Aspirin	10	11,027	11,037	9/10,000
Placebo	26	11,008	11,034	24/10,000

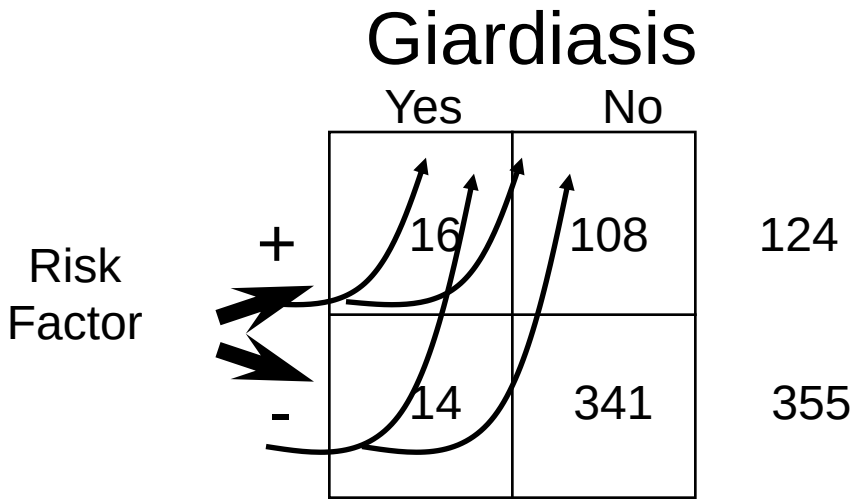
Risk Ratio (RR) = 9/24 = 0.38


Case-Control
Compare risk factor frequency.
cases
controls
Retrospective Cohort
Risk factor +
Risk factor -
Compare disease incidence.
Prospective Cohort
Risk factor +
Risk factor -
Compare disease incidence.
Clinical Trial
Treated
Not Treated
Compare disease incidence.
Past
Start of Study
Future

Key Differences Between Cohort & Case-Control

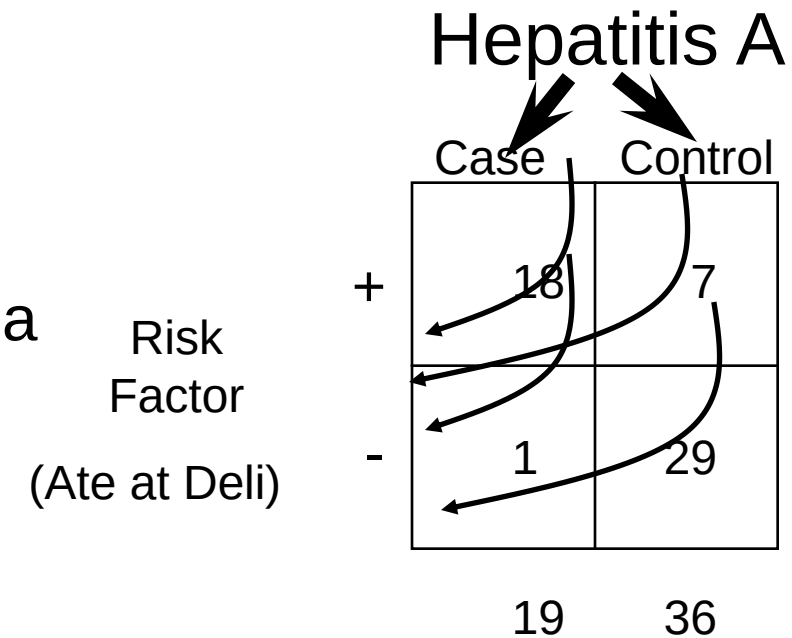
Cohort

Disease-free subjects are enrolled and then grouped by their exposure; then compare incidence.



Case-Control

Find diseased subjects and a non-diseased comparison group; compare odds of exposure.



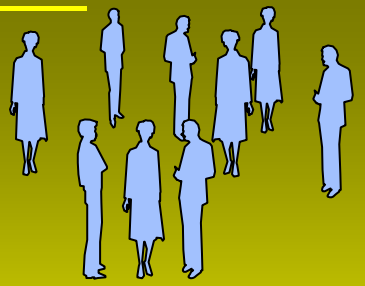
Identifying the Study Design

When reading a paper, it isn't always clear what the study design is. Sometimes there is a combination of strategies. However, you should think about what the predominant design features are.

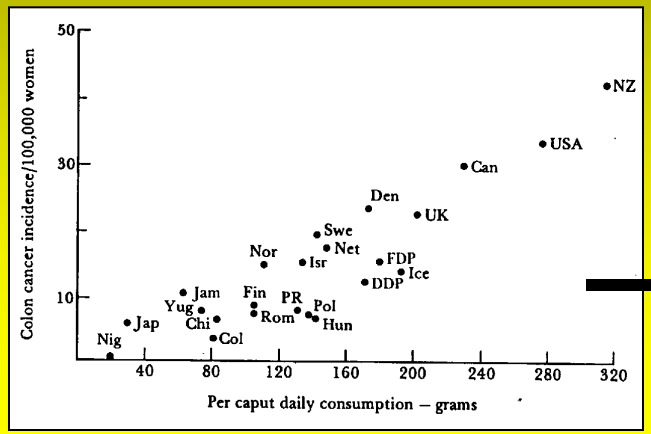
- Provides a framework for thinking about the study.
- Alerts you to weaknesses in some study designs.

Identifying the Study Design

Is it based on information about individuals?



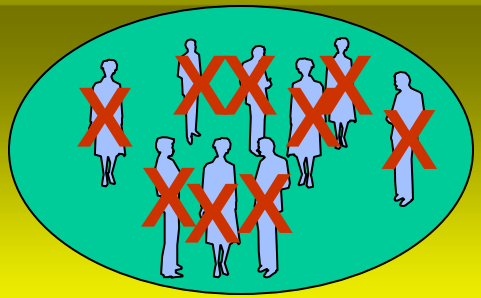
Or averages in populations?



Correlational (Ecologic)

Identifying the Study Design

Is there just one group?



8 people with bird flu

Did all subjects have the disease? (**Case Series**)

Did they evaluate presence of disease and risk factors at the same point in time?

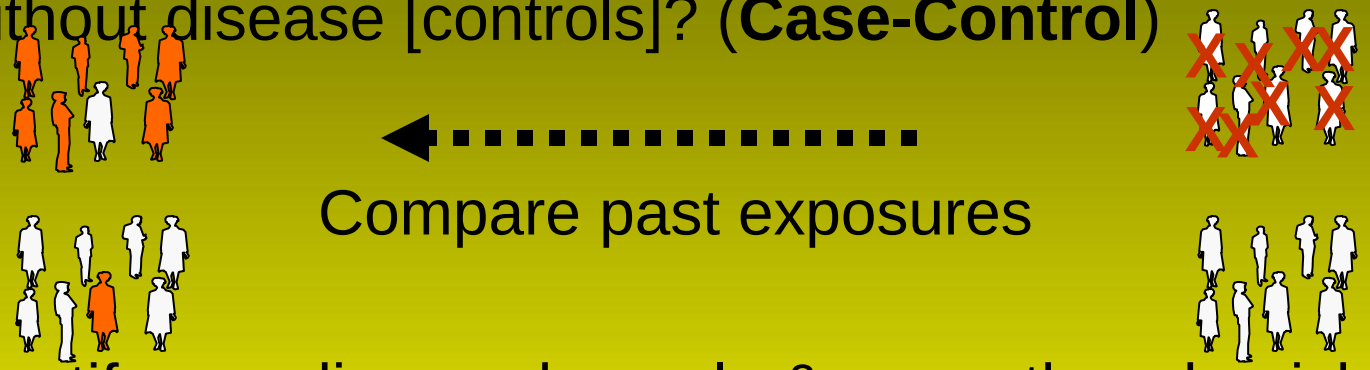
(**Cross-sectional Survey**)

Do you have heart disease?
Are you active?

Identifying the Study Design

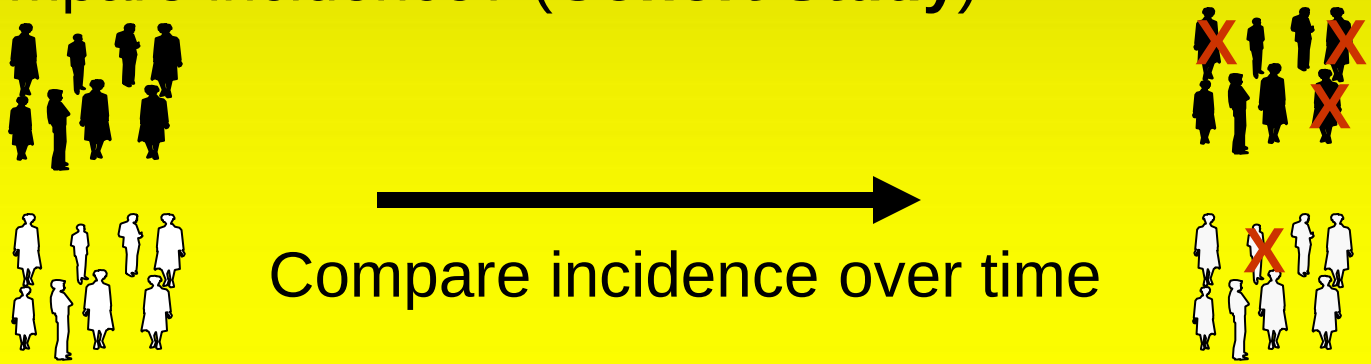
Two or more groups being compared?

- How were they selected? Did they find people with disease [cases] and then find a comparison group without disease [controls]? (**Case-Control**)



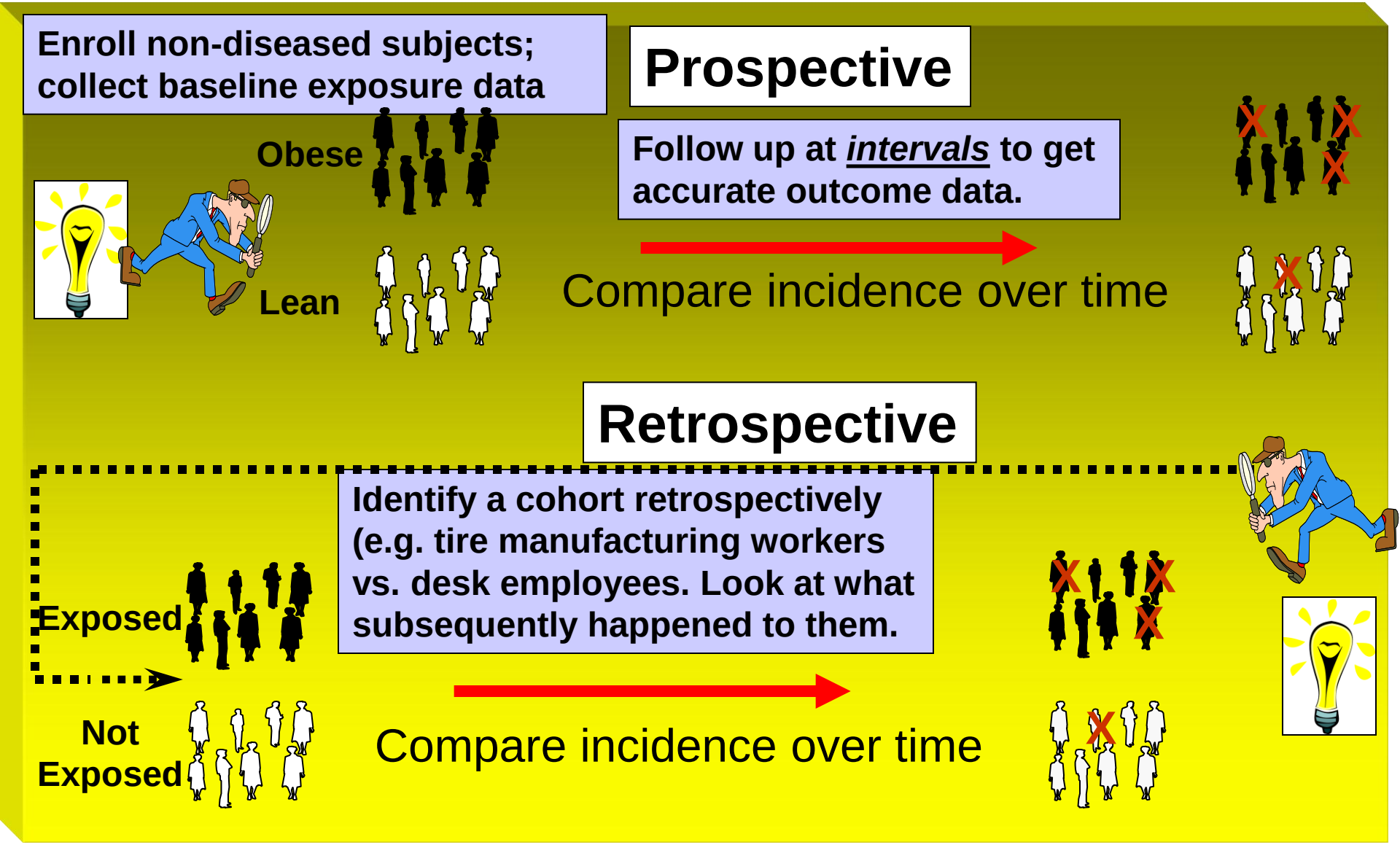
Compare past exposures

- Identify non-diseased people & group them by risk factor status? Then follow them longitudinally to compare incidence? (**Cohort Study**)



Compare incidence over time

In prospective cohort studies conception, design, & enrollment occur *before* anyone develops the outcome.



Identifying the Study Design

Did the investigators assign subjects to a treatment or intervention and follow them to compare outcomes? **(Clinical Trial)**

Compare incidence over time

Oral Contraceptives & Liver Cancer. Previous case reports of liver cancers in women on OCs. The authors contacted all cancer registries & collected information on all females with liver tumors.

OC Use ↓	Age Category 16 - 25 %	26 - 35 %	36 - 45 %
Yes	31	43	22
No	20	10	29
Unknown	49	48	49

1. Case series
2. Case-control study
3. Retrospective cohort
4. Prospective cohort
5. Randomized clinical trial

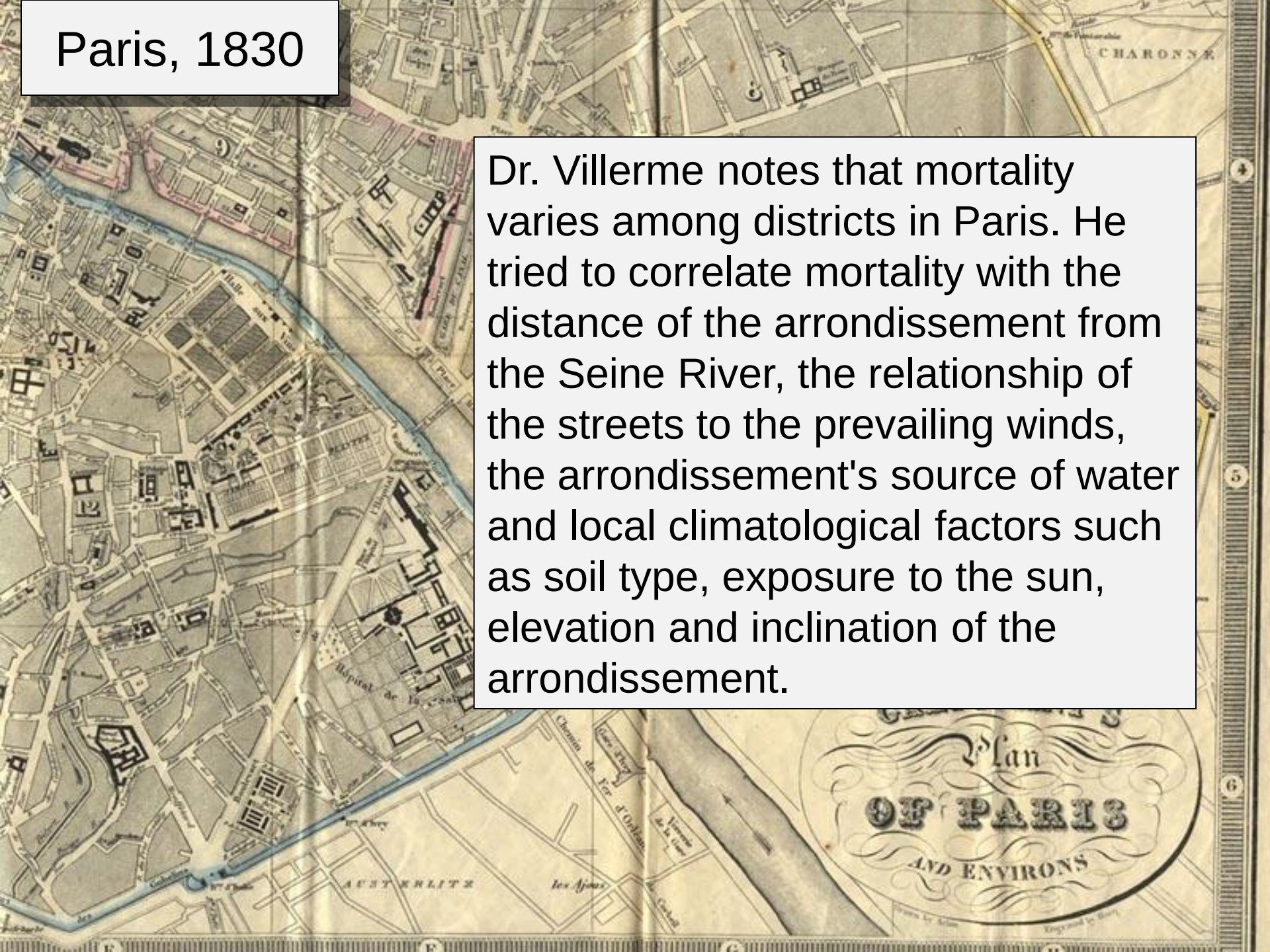
What kind of study was this?

State	Annual per capita Tobacco Sales	Lung Cancer Mortality Rate in 1965/100,000 pop.
Alabama	$600	92
Florida	$450	75
Georgia	$500	80
North Carolina	$550	66
Virginia	$400	45
Alaska	$200	35
Massachusetts	$150	33
New York	$175	20
New Jersey	$200	23
Rhode Island	$250	22

1. Case series
2. Case-control
3. Retrospective cohort
4. Cross-sectional survey
5. Correlational (ecologic)

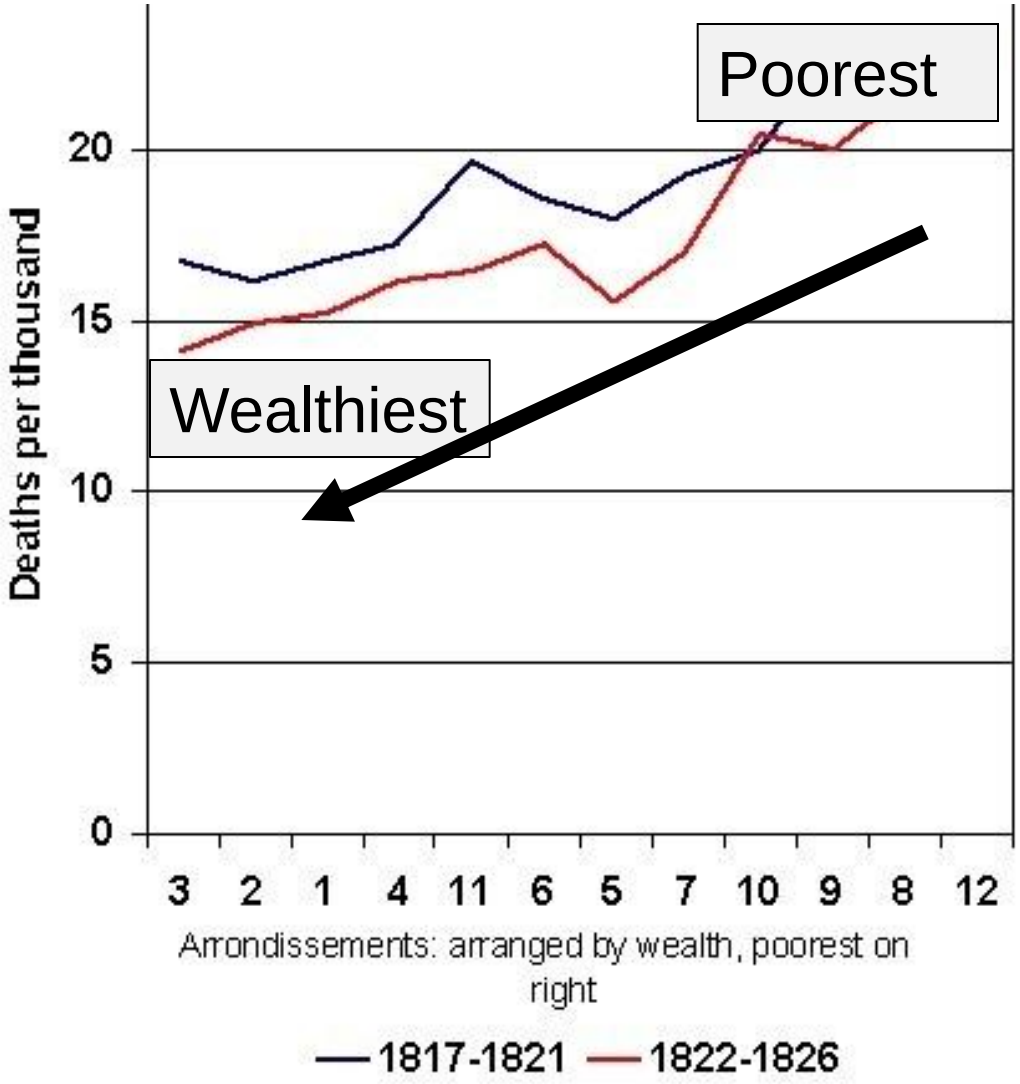
Type of study?

Paris, 1830



Dr. Villerme notes that mortality varies among districts in Paris. He tried to correlate mortality with the distance of the arrondissement from the Seine River, the relationship of the streets to the prevailing winds, the arrondissement's source of water and local climatological factors such as soil type, exposure to the sun, elevation and inclination of the arrondissement.

Villerme found that mortality correlated closely with the degree of poverty in the arrondissement (estimated as the % of people exempted from tax). The findings did not spark action.



Villerme found that mortality correlated with the degree of poverty in the arrondissement (estimated as the % of people exempted from tax). The findings did not spark action.

Type of study?

1. Case series
2. Case-control
3. Retrospective cohort
4. Cross-sectional survey
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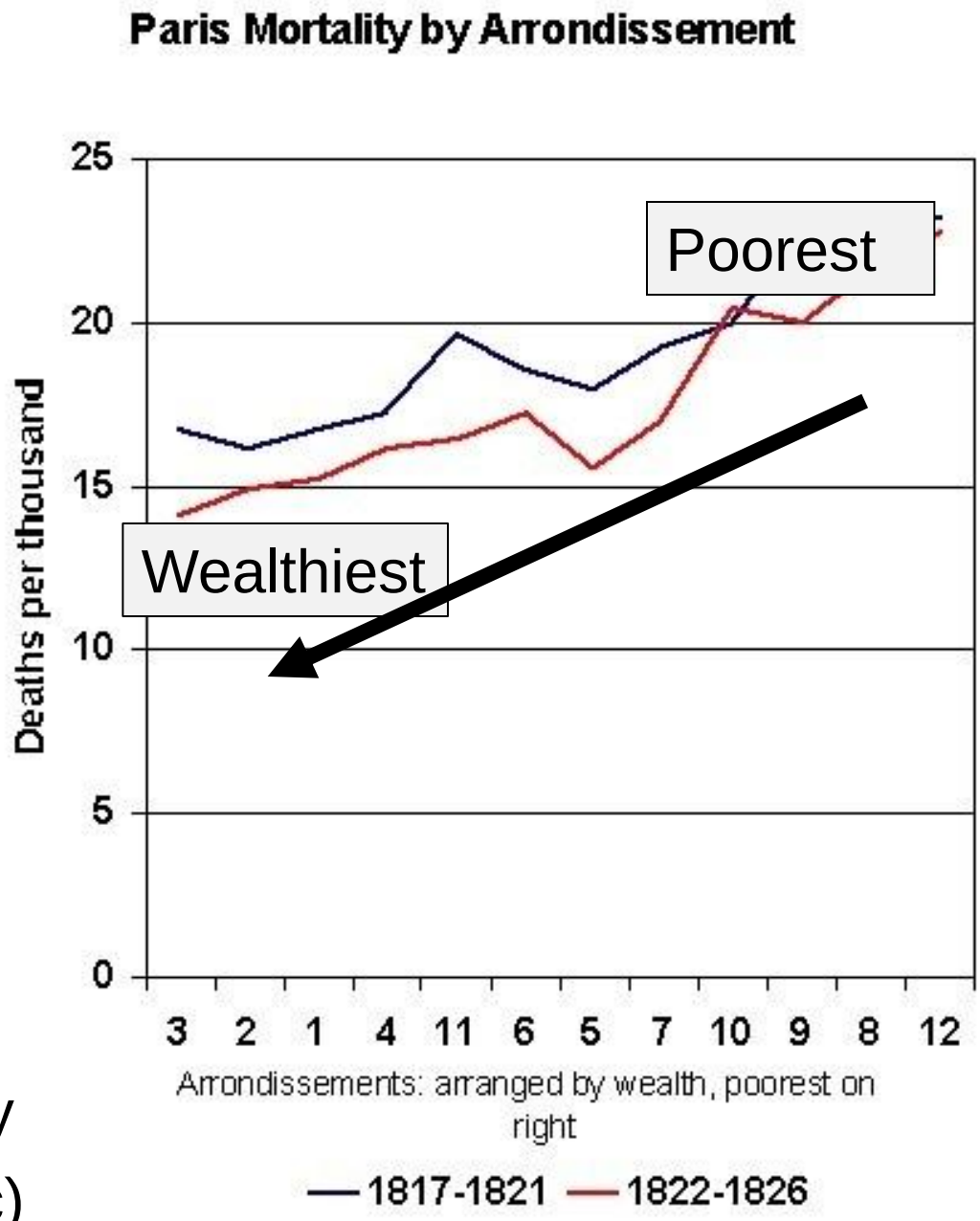
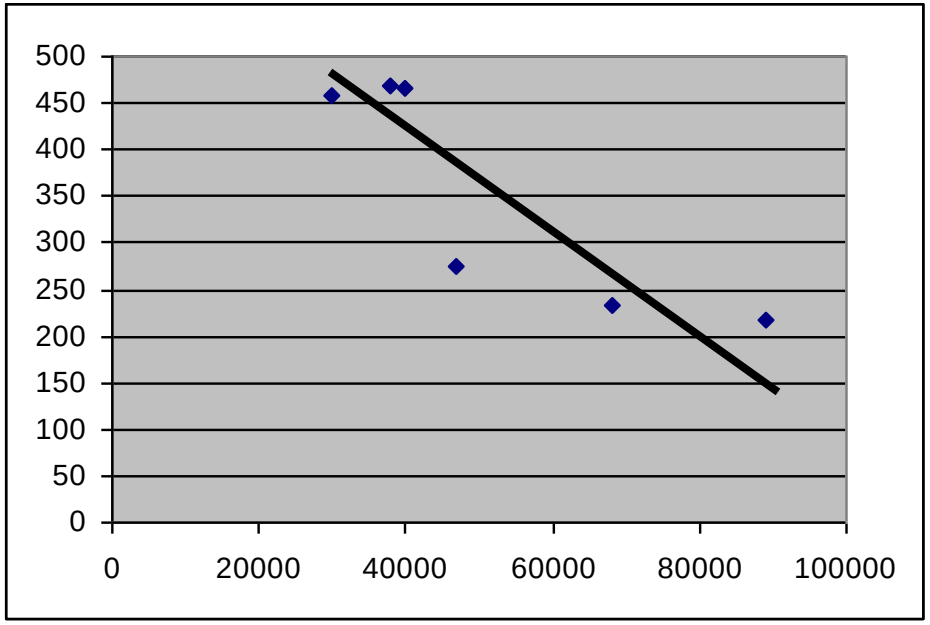


	Median Household Income	Premature Deaths /100,000
Lynn	38000	470
Lowell	40000	466
Springfield	30000	459
Newton	89000	218
Brookline	68000	233
Barnstable	47000	275



What kind of study was this?

Investigators in Bergen, Norway sent questionnaires about respiratory health, allergies, smoking habits, and occupational respiratory exposures to a random sample of residents between the ages of 15-70. After two reminders, 2,819 responses were obtained. Of these, 1,646 reported exposure to tobacco smoke from other members of their immediate family.

1. Case series
2. Case-control
3. Retrospective cohort
4. Cross-sectional survey
5. Correlational (ecologic)

A study in N. Engl. J. Med. examined whether eating a Mediterranean diet had any association with mortality in Greek adults. A baseline questionnaire was used to determine how closely the subjects followed a traditional Mediterranean diet, and the group was followed for 2 years, during which they determined the cause of death among all subjects who died.

Mediterranean Diet Score	Deaths in 2 yrs	Alive	Total
High (close adherence)	44	2586	2,630
Medium	61	3747	3,808
Low (poor adherence)	74	2383	2,457

1. Case-control
2. Retrospective cohort
3. Prospective cohort
4. Randomized clinical trial

What kind of study was this?

Bacteremia, Fever, and Splenomegaly Caused by a Newly Recognized Bartonella Species. *Eremeeva, et al.: N Engl J Med 2007;356:2381-7.*

A 43-year-old American woman developed a fever after traveling in Peru for 3 weeks. She visited Lima and Nazca and then traveled to the Sacred Valley of Urubamba, followed by Cuzco and Machu Picchu, where she hiked. She received numerous insect bites. Sixteen days after returning to the US she developed fever, insomnia, muscle aches, nausea, headache, and mild cough. At the hospital she was found to have anemia and an enlarged spleen (splenomegaly). Laboratory tests determined that her blood was infected with a genus of bacterium called Bartonella.

1. Case report
2. Case series
3. Case-control
4. Retrospective cohort
5. Clinical trial
6. Ecologic

What kind of study?

In 2003 a mass immunization against cholera was conducted in Beira, Mozambique. The following year there was an outbreak of El Tor Ogawa cholera in Beira. To assess the usefulness of the vaccine investigators compared the frequency of vaccination between persons with culture-confirmed cholera severe enough to have prompted them to seek treatment and age- and sex-matched neighborhood controls who did not have diarrhea.

1. Case series
2. Cross-sectional
3. Case-control study
4. Retrospective cohort
5. Prospective cohort
6. Clinical trial

Study type?

Risk of kidney failure associated with the use of acetaminophen, aspirin, and non-steroidal anti-inflammatory drugs. *Perneger TV, et al.*

People who take analgesic drugs frequently may be at increased risk of chronic kidney failure. These authors used a kidney dialysis registry to find 716 patients with kidney failure; they randomly selected 361 subjects without kidney disease from the same geographic area. They used phone interviews to estimate their cumulative past use of analgesics and compared the two groups.

1. Case series
2. Case-control
3. Retrospective cohort
4. Prospective cohort
5. Clinical trial

What kind of study?

Adiposity as Compared with Physical Activity in Predicting Mortality among Women. *Hu et al.: N. Engl. J. Med. 2004;351:2694-703.*

In 1976 the Nurse's Health Study enrolled 121,700 female RNs who completed a mailed questionnaire regarding their medical history & lifestyle. The women have returned follow up information every two years. This study grouped them by exercise level & BMI and compared mortality rates among different levels of these two risk factors.

1. Cases series
2. Case-control
3. Retrospective cohort
4. Prospective cohort
5. Clinical trial

Type of study?

Glucosamine, Chondroitin Sulfate, and the Two in Combination for Painful Knee Osteoarthritis.
Clegg, et al. N Engl J Med 2006;354:795-808.

Glucosamine and chondroitin sulfate are orally administered substances that have been used for years to treat joint problems in horses. Since they are relatively non-toxic there has been increasing interest in them for treating osteoarthritis, but there is controversy about their efficacy. These investigators randomly assigned 1583 patients with symptomatic knee osteoarthritis to receive 1500 mg of glucosamine daily, 1200 mg of chondroitin sulfate daily, both glucosamine and chondroitin sulfate, 200 mg of celecoxib daily, or placebo for 24 weeks. The primary outcome measure was a 20 percent decrease in knee pain from baseline to week 24. The primary outcome measure was whether the patient achieved a 20 percent decrease in pain as measured by the WOMAC pain subscale, a standardized, previously validity tool for assessing joint pain.

What kind of study is this?